

AIDS TO MEDICAL TREATMENT

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PREFACE TO THE FOURTH EDITION

THE present edition like its predecessors offers a concise and up-to-date summary of current medical therapeutics and again every effort has been made to retain its character as a useful working tool

Because of the ever increasing cost of production it was essential to reduce the size of the book, and special sections like dermatology and dietetics have had to be left to other volumes

I am indebted to many colleagues for suggestions and corrections. Dr John A Weaver revised the Tropical Diseases section and Dr Norman L Wright gave valuable assistance with the Infectious Diseases section. Messrs J H Restrick and G E McIlhagger in charge of Pharmacy at the Royal Victoria Hospital have as usual kept a firm eye on the posology. Dr Patrick Gorman has done yeoman service in proof reading and providing material on new methods and I am very grateful to him.

The Publishers have as always afforded every assistance and encouragement and I am filled with admiration for the very expert way in which the Aberdeen University Press have deciphered an unusually cryptic manuscript.

T H CROZIER

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CHAPTER I

CHEMOTHERAPY ANTIBIOTICS

Sulphonamides

Domagk drew attention to the bacteriostatic properties of sulphonamido-chrysoidin in 1935. His experimental work found clinical application in the use of sulphanilamide in puerperal sepsis. The brilliant results obtained in this field led to the elaboration of substituted compounds of *p*-amino-benzene sulphonamide. The original compound showed selective bacteriostatic activity against hæmolytic streptococci and coliform organisms. Later members of the series added to the list of bacterial infections which were controllable. Some have the further advantages of lessened toxicity, slower excretion, or where an intestinal bacteriostatic effect is required, lessened absorption. With the exception of this last group sulphonamides are rapidly absorbed from the small intestine and attain maximal blood concentration in about three to six hours. In order to maintain a bacteriostatic level in the blood it is therefore necessary to give the older preparations at four to six hourly intervals. Sulphonamides diffuse well into the tissues and this facility is of particular importance in treatment of meningeal infections where the concentration in the cerebrospinal fluid is about seven tenths of that in the blood.

Sulphonamides are excreted by the kidney after partial detoxication by the liver to an acetylated form which is not bacteriostatic and is comparatively insoluble. The rate of excretion varies according to the integrity of renal function and depends on the rate of urinary flow rather than on blood concentration. During transit through the renal tract sulphonamides are present in the urine in considerably higher concentration than in the blood (roughly thirty fold) hence their marked urinary antiseptic action in comparatively small dosage. There is danger of crystalluria and blockage of the

renal tubules, leading to anuria. Adequate fluid and alkali intake is therefore of cardinal importance during administration of these drugs.

If a mixture of sulphonamides be used instead of a single preparation this mixture by virtue of the different solubilities of the constituents and their acetyl products will not easily produce crystalluria. Blood concentration and therapeutic activity are enhanced by sulpha-combination. It has been found that a mixture of sulphadiazine, sulphathiazole and sulphamerazine (Trisulphonamide Tablets B.N.F.) is better than a combination of any two of these drugs. Cremotresamide (Sharp & Dohme) is a palatable suspension for children in which sulphathiazole is replaced by sulphacetamide.

The rapid disinfectant action of sulphonamides in the blood stream is not yet understood but the reaction is a bacteriostatic one with *p*-amino-benzoic acid as the essential link. This substance is necessary for the survival of micro-organisms and sulphonamides appear to compete with them for it. Direct chemical antiseptics count for little and there is neither increased immunological response nor recognisable phagocytic hyperactivity.

It is essential that sulphonamides be given in full dosage for a sufficient length of time otherwise there is danger of the infecting organism becoming sulpha resistant. This has been shown to occur frequently with certain organisms e.g. *Neisseria gonorrhoeae*.

There is no evidence that a synergistic effect follows the combined administration of sulphonamides and specific antisera. In cerebrospinal meningitis Mitman's statistics suggested that combined treatment yields less favourable results than sulphonamides alone.

Toxic effects of sulphonamides 1 *Headache depression nausea and vomiting*. These may be prominent with sulpha pyridine and appear at the beginning of treatment. On account of these symptoms this drug has been largely supplanted by newer members of the group. Vomiting leads to dangerous dehydration but may be minimised by giving the tablets powdered and suspended in milk or glucose and water. It is a sound rule to give twice the dose of citrate or

bicarbonate of soda with each administration. The fluid intake should be maintained at 4-6 pints daily and if there is excessive fluid loss through vomiting diarrhoea or sweating a substantial increase is indicated. Active delirium or frank psychosis sometimes complicates sulphonamide therapy and the drug must be withdrawn.

2 *Hæmaturia and oliguria* are manifestations of mechanical and reactive obstruction from crystal deposition in the renal tubules and pelvis. With the exception of sulphadiazine the newer compounds rarely cause trouble of this sort. Administration of the drug should cease and fluids and alkalis be given by mouth. The condition may progress to tubular necrosis and anuria which are unresponsive to these measures and require the treatment outlined on page 194.

3 *Drug fever* may present during the late stage of treatment by sulphonamides and be mistaken for a relapse.

4 *Cyanosis* is harmless it may be due to methæmoglobinæmia or rarely to sulphæmoglobinæmia.

5 *Skin rashes* may appear during or after treatment the commonest being a morbilliform eruption. Rashes resembling erythema nodosum are sometimes seen seven to twenty days after completion of treatment. Polyarteritis nodosa is believed to follow sensitisation by sulphathiazole. Careful watch should be kept on the blood counts of patients who have shown dermal sensitivity.

6 *Hæmatological complications* Acute hæmolytic anæmia with or without jaundice leucopenia and agranulocytosis have resulted from treatment by these drugs.

Cross sensitivity Dosage or contact with a chemical may sensitise the individual to it and to many other related but dissimilar compounds. Drugs containing a *para* amino grouping are particular offenders in this respect. Cross sensitivity between local anaesthetics aniline dyes saccharin sulphanilamide and accelerators used in rubber manufacture has been reported. Procaine and its penicillin salt sulphonamides PABA and PAS are common therapeutic currency today and there is the likelihood of pre sensitisation by hair dyes, sunburn lotions etc. It is thought that dermatitis and

granulopænia arising after sulphonamides may be due to cross sensitisation rather than intrinsic sulphatotoxicity

Parenteral administration Sodium salts of sulphadimidine (Sulphadimidine Sodium Injection BP) sulphamerazine sulphathiazole and sulphadiazine are soluble and may be given by deep intramuscular or (better) intravenous injection. They are alkaline and irritant but are very useful for the initiation of treatment in serious cases in unconscious patients or where uncontrollable vomiting frustrates oral medication. In cerebrospinal fever much depends on securing rapid action of the drug and one third to half of the loading dose should be given into a vein.

These preparations must not be injected into the theca or other serous cavity. They may be given undiluted deeply into the buttock for intravenous use they should be diluted to 20 ml with distilled water and introduced slowly. Adequate fluid intake is as important with injected as ingested sulphonamides.

Local application The more soluble sulphonamides have been used on infected skin or connective tissue lesions. Sulphacetamide forms a non irritant sodium salt and 10-30 per cent solutions are used in ophthalmic and nasopharyngeal work. Powders containing potassium penicillin and a sulphonamide have been found valuable in treatment of infected wounds, ulcers and pyogenic dermatoses. Care should be taken to minimise contact with surrounding healthy skin.

Sensitisation is common with prolonged local application and a spreading eczematous rash on the skin surrounding the site of application is the first sign. Catastrophe may attend subsequent local or general administration of sulphonamides and indiscriminate topical use is therefore to be deprecated.

Organisms Sensitive to Sulphonamides

Hæmolytic streptococci Pneumococci Esch coli N gonorrhæe N meningitidis H pertussis and influenzae (some strains) H ducreyi Sh dysenteriae

With regard to sulphonamides which are used for their bacteriostatic action in the bloodstream sulphanilamide is as good as the newer preparations against streptococcal and

coliform infections. In practice the choice lies between sulphadiazine, sulphadimidine, sulphamerazine and sulphafurazole. These are comparatively slowly excreted, allowing smaller dosage or longer intervals once the initial effect has been achieved. This is true especially of sulphamerazine. Sulphadimidine and its acetyl derivatives are freely soluble and do not crystallise readily. Sulphamethoxypyridazine (Lederkyn, Lederle, Midcal, P.D.) a recent introduction is excreted slowly and is effective in small dosage (0.5 G twice on the first day and once daily thereafter).

For cases of average severity the adult dosage of sulphadimidine is 2 G followed by 1 G four hourly for two to five days. On the day after defervescence occurs the intervals may usually be increased to six hours. In more serious cases this dosage should be increased by 50-100 per cent until a satisfactory response has been obtained. Night dosage must be insisted upon until the brunt of the infection has passed. In cases of severe infection 1.2 G of an ampoule preparation should be given (diluted to 10-20 ml with sterile distilled water) intravenously at the outset and if necessary 1 G doses may be repeated intravenously at intervals of four hours until effective oral dosage can be established.

For moderately severe cases in children the following dosage scheme is applicable:

	0-6 months	6 months 5 years	5-10 years
First dose	0.5 G	0.5 G	1.0 G
4-hourly for 2 days	0.25	0.5	0.75
6-hourly for 2 days	0.25	0.5	0.5
6-hourly	0.125	0.25	0.5

These may be prescribed in suspension form, e.g. Sulphadimidine Mixture for Infants B.P.C. (1 drachm = 0.5 G).

The principles governing the administration of sulphonamides may be recapitulated thus:

An exact diagnosis is desirable before embarking on therapy but treatment should not be withheld for the results of bacteriological tests.

Except when used prophylactically sulphonamide treatment should rarely be continued for more than seven to ten days. If good response is not forthcoming within two to three days eventual success is unlikely and the case should be reconsidered.

Fluid (4-6 pints daily for adults) and alkali intake must be ensured.

The urinary output must be watched and a test for albumin made daily.

The leucocyte count must be watched when large doses have been given or signs of sensitivity have appeared. The smaller the daily dose the less likely is sensitisation to arise regardless of the duration of treatment.

The poorly absorbed sulphonamides Succinylsulphathiazole and phthalylsulphathiazole exert a bacteriostatic action on the intestinal flora without achieving effective concentration in the blood. They have some utility in bacillary dysentery, infective enteritis and ulcerative affections of the colon. Combination with sulphadiazine gives better results. In colonic surgery the risk of infection from leakage of bowel content is ever present. By the use of these drugs the bacterial count of the stools may be markedly reduced. A popular antibacterial routine for bowel surgery is a succinyl sulphonamide for seven days pre-operatively with streptomycin on the last two days and a phthalyl sulphonamide post-operatively. Neomycin is also effective for this purpose.

Average adult dosage

Succinylsulphathiazole 16 G then 3 G four hourly
(Absorption less than 5 per cent. Causes liquid stools of small bulk.)

Phthalylsulphathiazole 3 G and 2 G six hourly for two days then 1-1.5 G six hourly for four to six days
(Absorption less than 5 per cent. More actively bacteriostatic than the above mentioned. Does not tend to liquefy the stools and is therefore more effective in dysentery.) *Phthalylsulphacetamide* In similar dosage.

Prophylactic use Sulphonamides have been used over periods of weeks or months for prevention of upper respira-

tory infections particularly in rheumatic subjects. Penicillin is now considered to be a better prophylactic but good statistical results have followed the administration of sulphadiazine 0.5 g daily throughout the winter months in rheumatic cases. Toxic skin and bone marrow reactions have been rare.

Penicillin

The series of brilliant researches which culminated in the commercial production of penicillin originated in an observation by Fleming in 1928 that a portion of a blood agar plate which had been accidentally contaminated by spores of a mould *Penicillium notatum* contained a diffusible substance which was markedly inhibitory to the staphylococcus with which the plate had been seeded and filtrates were found to be no more toxic to living tissues than the broth medium in which the mould had been grown. The problem of concentrating penicillin was taken further by Florey who achieved thousand fold concentrations and demonstrated its *in vivo* antibiotic virtue.

Penicillin is an organic acid which has been synthesised but commercial manufacture is by extraction from cultures of *P. notatum*. The several forms of penicillin differ slightly in structure and in antibacterial activity. The free acids are unstable in aqueous solution hence the use of their sodium salts which are freely soluble and relatively stable. Pharmaceutical preparations are made almost entirely from benzyl penicillin salts and the sodium salt has a potency of over 1600 i.u. per mg.

Penicillin is unstable in the presence of heat, moisture, acids and alkalis and is inactivated by the enzyme penicillinase which is elaborated by certain bacteria. Only redistilled sterile water should be used as solvent and great care taken to avoid contamination of the solution. The sodium salt is hygroscopic and calcium and potassium salts are therefore used in preparation of tablets, powders etc.

Penicillin acts by preventing synthesis of a component of the bacterial cell wall. It exerts a powerful bactericidal influence on micro-organisms particularly during the phase of active growth and multiplication possibly by interfering

with the availability or assimilation of essential nutrients such as the sulphhydryl groups of certain amino-acids

The question of sensitivity and resistance to antibiotic drugs is a difficult one. With regard to penicillin some organisms such as certain streptococci and pneumococci appear to retain their sensitivity indefinitely and infections with these can be controlled with the usual blood concentrations of the drug (about 0.10 i.u. per ml) whereas with other organisms e.g. *Str. viridans* a four fold concentration may be necessary. Induced resistance has been noted in the case of *Staphylococcus aureus* and there has been a progressive increase in penicillin resistant strains encountered in hospital in patient practice.

Superinfection. It has been found that when considerable clearance of organisms results from antibiotic therapy unusual and resistant flora may appear doubtless as a result of symbiotic imbalance. Coliform organisms and fungi are commonly found in the respiratory tract following penicillin therapy and fatal staphylococcal enteritis has followed successful tetracycline therapy.

Combination of antibiotics. Antibiotics may be divided into two groups

1 *Bactericidal drugs* Penicillin streptomycin neomycin bacitracin Sulphonamides although not bactericidal have synergistic affinities with this group

2 *Bacteriostatic drugs* Chloramphenicol and the tetracyclines

Pairs of drugs from the same group or from both groups may exhibit additive synergistic or antagonistic activity. Those in the first group usually show a synergistic effect and in clinical practice penicillin has been found effective in combination with streptomycin and with sulphonamides for infections resistant or partially sensitive to each alone. Drugs of the second group usually show an additive action which ordinarily is of little advantage. Combinations of pairs from different groups produce variable results depending on whether the infecting organism is sensitive to the bactericidal or the bacteriostatic drug. In the first case the effect is antagonistic as the bactericidal drug acts only against multiplying organisms while bacteriostatic preparations inhibit growth.

in the second if the organism is inhibited by very large doses of the bactericidal agent the combination will show a synergistic response. In general it is undesirable to combine agents of different groups nevertheless it is likely that each antibiotic has its own particular mode of attack and in highly resistant cases it would seem rational to use them in series and in descending order of preference.

Blood levels **Duration of antibiotic effect** After a normal intramuscular dose of benzylpenicillin the concentration in the blood rises steeply but falls below the useful therapeutic level in about four hours. A dose of the order of $1\frac{1}{2}$ mega units will give an effective concentration for about twenty-four hours. Much ingenuity has been expended in prolonging the therapeutic blood level although it is not certain that this is necessary in all cases.

Attempts have been made to prolong effective penicillin blood levels by the use of blockade substances which hinder excretion of the antibiotic by the renal tubules. A propylsulphamyl benzoic compound (Benemid Sharp & Dohme) has proved an efficient adjuvant to high level dosage with penicillin in septicæmic states such as *Str. faecalis* and staphylococcal endocarditis where conventional antibiotic therapy had failed. Dose 0.5 G six hourly orally.

Crystalline penicillin (2.8 mega units daily) by three hourly intramuscular injection is used for serious infections e.g. septicæmia meningitis. For a case of moderate severity the choice lies between crystalline penicillin (1.2 mega units daily) intramuscularly and daily or twice daily injection of a prolonged action preparation such as a procaine potassium salt which is relatively insoluble and maintains an effective serum level for about sixty hours. The usual dose is 300 000-600 000 i.u. daily.

Phenoxymethylpenicillin (Penicillin V) is stable and resistant to gastric acidity and is consequently reliable by the oral route. Combined with probenecid (Benemid) high and sustained serum levels are reached despite the fact that urinary excretion amounts to only 25 per cent. of the ingested dose. Penicillin V (e.g. Distaqueam V K) has obvious advantages in children and many adults. Its use has not been routine in the most serious infections although L. Quinn

have given good results in *H. influenzae* meningitis in meningitic states intrathecal streptomycin medication may be desirable initially in addition to systemic dosage

Resistance to streptomycin is developed by all micro-organisms with great facility so that its use has been abandoned where any other antibiotic will serve and its main role is in tuberculous infections. Resistance can be delayed by employment of adjuvant drugs such as *para* aminosalicylic acid the thiosemicarbazones and isoniazid. Adult dosage is 1 G daily by intramuscular injection this is optimal as regards good therapeutic response with minimal toxicity

The Tetracyclines

Chlortetracycline Aureomycin combines relative freedom from toxicity with a wide range of antibiotic activity. It has proved effective against Gram positive and Gram negative organisms as well as viral and rickettsial agents and it possesses a further advantage of activity by the oral route. Most of the organisms shown as sensitive to penicillin and streptomycin are sensitive to tetracyclines also. The drug is particularly useful against *Staphylococcus aureus* and *Str. faecalis* and haemophilus infections usually respond. Good results have been reported in virus and rickettsial infections in tularemia actinomycosis and bartonellosis.

This antibiotic is an effective alternative in cases when injections are undesirable where antibiotic resistance has developed or in mixed infections e.g. of the urinary tract. It has been employed with success in severe surgical infections such as peritonitis for such intravenous administration (50 mg followed by 25 mg six hourly for six days) is indicated in addition to mouth dosage. For cases of moderate severity the adult oral dose is 0.25 G six hourly (children 10-15 mg per kg body weight) for seriously ill patients double dosage should be used for a few days and perhaps one or more intravenous priming doses. Chlortetracycline is used locally for ophthalmic inflammatory conditions and ointment and drops are available.

Toxic effects are slight nausea abdominal cramps and diarrhoea leading to eczema of the perianal region have been encountered (staphylococcal or monilia superinfection)

Raw tongue and sore mouth are frequent complications of oral antibiotic therapy. These side effects are lessened by vitamin B and C concentrates, buttermilk, yoghurt and lactic cheese. Enpac, Lloyd Hamol is a very useful acidophilus preparation which contains antibiotic resistant strains.

Oxytetracycline (Terramycin) was isolated by Finlay from cultures of *Streptomyces rimosus*. This substance possesses similar therapeutic properties to the other tetracyclines. It is active against coral infections and appears to have a useful rôle in staphylococcal, streptococcal and pneumococcal infections. It has been given with success in virus pneumonia, brucellosis, spirochetal and rickettsial infections and gonorrhoea. Surgical infections such as peritonitis and gas gangrene are reported amenable to its action. Like the other broad spectrum antibiotics, oxytetracycline does not readily induce bacterial resistance. Another feature common to the group is chemical stability: much of the ingested dose is active in the intestine, causing effective clearance of pathogenic and other flora.

Toxic effects are of the usual oro-gastro-intestinal variety.

Oxytetracycline is available as hydrochloride and oral dosage is of the order of 10-15 mg per kg body weight daily in fractional doses at six-hourly intervals (for the average adult 1.2 G daily). Ampoules for intravenous therapy are available (250 and 500 mg) and they may be added to intravenous drips in cases of overwhelming infection and where the intestinal side-effects would be undesirable. Local applications have been used in ophthalmic practice.

Tetracycline (Achromycin) represents the molecular structure common to chlortetracycline and oxytetracycline and has been prepared by dehalogenation of the former drug and by mould culture. The activity pattern of the three tetracyclines is essentially similar although they differ in chemical stability: complete cross-resistance has been noted between them *in vitro*. Adult dosage: 250 mg tetracycline hydrochloride orally six hourly. The drug is well tolerated intravenously. It causes less intestinal upset than the others.

Chloramphenicol (Chloromycetin) was obtained from *Streptomyces venezuelae* cultures by Ehrlich and Burkholder in 1947 and was later synthesised. Like the tetracyclines

chloramphenicol is a broad spectrum antibiotic active against many Gram positive and Gram negative pathogens as well as viral and rickettsial organisms. It is particularly valuable in treatment of infections of the typhus and typhoid groups. Good results have followed its use in salmonella and dysenteric conditions, pertussis, urinary infections, pneumonia (coccal and viral), relapsing fever, *H. influenzae*, meningitis, parotitis and lymphogranuloma venereum. Chloramphenicol is rapidly absorbed from the bowel, widely distributed in the body tissues and excreted by the kidney. It appears in effective concentration in the cerebrospinal fluid, being excreted in an inactive form in the bile and urine. It is not a useful agent against infections of these media.

Side effects are nausea, flatulence and diarrhoea. Angular stomatitis and desquamative glossitis are not uncommon. Anal and vaginal irritation occasionally occur, as with the tetracyclines. These manifestations are believed to be due to superinfection with fungi, mostly *Candida albicans*. Toxic effects on the bone marrow have been reported, ranging from mild anaemia to agranulocytosis and aplastic anaemia. These have appeared mostly in patients who have had repeated courses of the drug.

Chloramphenicol is effective as a topical medicament, particularly in otitis media and mastoid wounds. Solutions in propylene glycol for aural use and drops for ophthalmic use are available. Oral dosage, adult 0.25 G, six hourly for five days; larger amounts may be necessary in severe infections, e.g. typhoid. The drug has a bitter taste, hence the popularity of Chloromycetin Palmitate P.D., a pleasantly flavoured suspension containing 125 mg per ml. Ampoules are useful in emergency (intravenously 2 ml = 0.5 G).

Polymyxin

This includes five related polypeptide antibiotics derived from cultures of *Bacillus polymyxa*, of which three like most antibiotics of bacterial origin are nephrotoxic. Polymyxin B and E are largely free from this disadvantage. Their action is bactericidal and acquired resistance is not of practical importance. Polymyxin B is in commercial production. It has been proved effective against *Ps. pyocyanea* which may

be pathogenic in burns and has become a common residual infecter after use of other antibiotics. Its action is less marked against *Proteus*, *Pseudomonas* and *Coli aerogenes* infections of the urinary tract. Dosage is 2.5 mg per kg body weight intramuscularly daily according to the integrity or otherwise of renal function. Topical application is useful for burns and superficial infections.

Erythromycin

Isolated from a soil organism (*Streptomyces erythreus*) this medium spectrum antibiotic is effective against most Gram positive invaders also neisseriae, haemophilus, spirochaetes and rickettsias. It has therefore similar validity to penicillin although possibly more active against staphylococci and *C. diphtheriae*. Oral dosage (1.2 G daily by six hourly fractions) suffices and toxic manifestations beyond gastro intestinal upset are rare. Unfortunately organismal resistance is rapidly acquired and erythromycin should not be used alone in chronic infections like bacterial endocarditis and osteomyelitis. Termination of the diphtheria carrier state has been reported (N. Wood and E. M. R. Hemphill 1957).

Carbomycin possesses similar but lesser activity to erythromycin and cross resistance occurs.

Spiromycin, Rovamycin is also related to erythromycin has a similar field of activity and cross resistance has been demonstrated.

Oleandomycin, Matromycin is similarly related and has analogous effects including cross resistance.

Novobiocin, Albamycin also belongs to this group. The dose is 1.2 G daily orally. Favourable reports have arisen of its use in bronchitis, pneumonia and staphylococcal soft tissue infections.

Vancomycin

This antibiotic is not yet generally available and so far has been used intravenously. It is reported little toxic, bactericidal not productive of cross resistance and with a therapeutic spectrum similar to penicillin. It may prove valuable in severe and resistant staphylococcal infections. Dose 0.5 G six hourly by mouth for its oral intestinal effect or intravenously where systemic antibiosis is required.

Neomycin

A stable antibiotic obtained from cultures of *Streptomyces fradiae*. Particularly effective against *Klebsiella pneumoniae*, *Haemophilus*, *Pseudomonas* and *Proteus* groups. Organismal resistance rarely presents and sensitivity reactions are infrequent. For pre-operative intestinal antiseptics 1 G of neomycin sulphate is given by mouth four hourly for two to three days. Intramuscular dosage (under skilled supervision) is used for severe systemic infections and urinary tract infections insensitive to other antibiotics e.g. staphylococci, enterococci. Dose not exceeding 15 mg per kg body weight daily or 1 G in all by six hourly injections. Renal function should be carefully watched.

Nystatin

An anti-fungal preparation from cultures of *Streptomyces noursei*. Has been used locally against fungal and yeast infections of the skin and mucous surfaces.

CHAPTER II

INFECTIOUS DISEASES

Enteric Fever

The treatment of typhoid and paratyphoid infections is similar. In this country the latter are usually of a mild nature but their importance as a Public Health problem remains.

Enteric cases should as a rule be treated in isolation hospitals if circumstances demand home treatment adequate facilities for segregation and the services of a day and night nursing staff will be required. The successful issue of a severe attack depends largely on skilful nursing; the typhoid sufferer by reason of his long and exhausting illness requires devoted and unremitting care. The nursing personnel should have had prophylactic inoculations.

Comfort, quiet and convenient isolation facilities are important considerations in the selection of the sick room. Unnecessary furnishings and absorbent floor coverings should be removed. In cool climates an open fire provides cheerful warmth and soiled wipes and dressings can be easily disposed of by burning. The room temperature should be kept at 60-65° F. Fresh air is important but the window openings should be screened with cotton mesh to exclude flies. Visitors should not be allowed into the sick room.

A single bed with a firm mattress preferably of sponge rubber or of the interlock spring type makes nursing routines easier. Food utensils, crockery and cutlery should be reserved exclusively for sick room use and may be sterilised after cleansing by boiling or by immersion for twenty minutes in a hot 2 per cent solution of bleach powder. Soiled linen is disinfected by soaking in 5 per cent phenol for twelve hours before being washed. The use of a public laundry is illegal. Stools, urine and sputum should be treated with a liberal amount of 5 per cent phenol or 2½ per cent

lysol or cresol for two hours before disposal Gauze wipes lint or cellulose tissues may be used instead of handkerchiefs and afterwards burnt

During the febrile stage the patient is encouraged to lie quietly and do nothing for himself but frequent changes of posture are essential in order to minimise the risk of pressure sores and pulmonary congestion The toilet of the mouth and skin must be meticulously attended to and the sacral and buttock areas should receive treatment after every bowel movement

Diet Patients usually benefit from an initial alimentary rest and this may be ensured by allowing fluids only

Secway barley water albumin water home made lemonade or fruit juice sweetened with glucose should be given freely fruit jellies are a pleasant variant Fruit drops and barley sugar promote salivation and help to maintain caloric requirements A daily fluid intake of at least 4 pints should be aimed at

After two or three days milk may be added (2-3 pints daily) and this should be given in two-hourly feeds by day and may be plain or flavoured with tea coffee cocoa Horlick's Prosol or Benger's according to the patient's preference If milk causes colic or flatulence or if the stools show evidence of poor digestion (curds) it should be withdrawn for a day or two and then given peptonised citrated or diluted with lime water

By the middle of the second week or earlier if diarrhoea is not troublesome the dietary may be gradually increased by the addition of soft foods such as Farex junket custard puddings milk shapes made with cornflour or gelatin beef tea and chicken jelly Further additions such as lightly cooked eggs pounded fish and chicken strained soups apple tomato and prune purees porridge thin slices of bread and butter with jelly preserves plain biscuits and sponge cake may now be made

When the third week is over defervescence complete and abdominal hazards safely negotiated the diet may be more liberal but still bland indeed most authorities use a high caloric diet from the outset Boiled or steamed fish minced beef sieved vegetables such as spinach carrots parsnips

cauliflowers and tomatoes may be cautiously added. Thereafter there may be gradual return to a full normal diet.

The stools should be inspected daily throughout the febrile stage; much useful information can thus be gained as to the suitability of the diet. Abdominal pain, distension, frequent loose or foul stools, or the presence of curd masses or undigested food material are indications for temporary pruning of the dietary.

Chemotherapy. Sulphonamides and penicillin are of no value except in treatment of secondary infections such as pneumonia and parotitis. Impressive results have been obtained from chloramphenicol therapy. The pyrexial period is shortened to three or four days and the duration of infectivity, as judged by bacteræmic evidence, to about five days. Relapse occurs if the total dosage is inadequate, but this is as a rule readily controllable by further treatment. Dosage 0.5 G initially and then 0.25 G two hourly orally until the patient becomes afebrile, when the interval may be increased to four hours for the next five days. The average medication is 16 G over six days. Cases coming late to treatment show less satisfactory response and may require double dosage over the first five days. The risk of perforation and hæmorrhage persists in some degree despite rapid clinical improvement and it is important that exertion and diet be strictly controlled for several weeks after defervescence.

Complications

Restlessness, insomnia, delirium and hyperpyrexia may be prominent during the second and third weeks. Repeated tepid sponging, soothing and can be carried out with little disturbance. Insomnia often yields to phenobarbitone gr 1/2 but active delirium may require morphine gr 1/4 with hyoscine gr 1/10 subcutaneously.

Constipation rarely requires active treatment and is best corrected by dietetic modification. If prolonged liquid paraffin or a simple enema may be ordered.

Diarrhœa cannot as a rule be controlled by astringents and should be countered by dietetic restriction. If severe starch and opium enemata or gr 10 of Dover's powder may be

tried late in the evening to encourage sleep. Meteorism can often be relieved by passage of a rectal tube or by a small saline enema. Toxaemia may be profound and accentuated by dehydration. The best treatment is an intravenous glucose saline drip (2-4 litres in twenty four hours). If exhaustion is marked, a litre of blood should precede the glucose saline.

Intestinal haemorrhage calls for reduction of the diet to sips of water and a hypodermic injection of morphine gr $\frac{1}{4}$. If at all severe or prolonged blood transfusion must be given. Intestinal perforation is a most serious complication and its presence may be masked by haemorrhage. Immediate operation should be undertaken. Mouth feeding is stopped and morphine given as soon as the diagnosis is established. Chlortetracycline by vein is most effective against peritonitis.

Cardiac and circulatory failure are problems for which no adequate solution is available. Raising the foot of the bed and bandaging the limbs will help to combat peripheral circulatory failure. Injections of nikethamide or caffeine sodium benzoate may be given but an intravenous drip containing norepinephrine and hydrocortisone is best. Pneumonia and bronchopneumonia require energetic treatment by penicillin or a tetracycline. Phlebitis calls for immobilisation of the affected limb and warm packs are useful for relief of pain. Carefully controlled anticoagulant therapy may be instituted provided that the risk of intestinal haemorrhage has passed. Heparin in 5 000-unit doses intravenously thrice daily for three to five days is probably safest. Vein trauma may be minimised by use of an indwelling needle of the Gordh type.

Convalescence

Convalescence should be slow. Modified rest in bed is maintained for two or three weeks after the temperature has become normal. The appetite is usually good and should be satisfied by a bland high-calorie diet on which the convalescent may regain body weight and energy. A lazy holiday by the seaside or in the country will hasten recuperation.

Prophylaxis

1 Notification

2 Strict isolation of patients until three consecutive weekly stool and urine examinations are negative for the enteric group of organisms. Persistence of V_i agglutinins is presumptive of the carrier state and the stools and urine should be cultured twice weekly for three weeks. Disinfection of dejecta and fomites. Attendants should wear rubber aprons and gloves and be conscientious in regard to washing their hands after attending to the patient. Terminal disinfection of the patient and sickroom (the patient should be given a bath, shampoo and complete change of clothing before being liberated). Preventive inoculation and daily observation of contacts. Opinion is divided regarding the utility of inoculating contacts with T A B vaccine.

3 Public Health measures include bacteriological control of water and food supplies, efficient sewage disposal, fly prevention, search for source of infection, detection and treatment of carriers. Employees of waterworks, dairies and personnel engaged in the handling of foodstuffs should have periodical bacteriological and serological examination to exclude the carrier state. Carriers should be educated so that they may not jeopardise the lives of their neighbours. If evidence of gall bladder damage is forthcoming, cholecystectomy will often terminate the carrier state. Urinary carriers are more difficult and nephrectomy may be necessary in the presence of an extensively diseased kidney. The results of antibiotic therapy have been disappointing.

4 Inoculation of exposed populations with T A B vaccine. Alcoholised vaccines cause less undesirable reaction and produce better immunity than the heat treated and phenolised types. They usually contain *Salmon typhosa* 1 000 million, *Salmon paratyphi* A and B of each 750 million per ml.

Dosage	Adult males	Adult females	Children under 3 yrs
Initially	0.5 ml	0.2 ml	0.05 ml
After 3 weeks	0.5 ml	0.4 ml	0.1 ml
Annually	0.25 ml	0.2 ml	0.1 ml

Dosage of phenolised vaccines is double the above.

If rigidly adhered to this routine usually affords an immunity to clinical typhoid which is impregnable to all except massive infections. Sub-infection with development of the carrier state sometimes occurs.

5 During outbreaks of enteric drinking water and milk should be boiled and raw fruit vegetables ice cream and shellfish avoided unless their source is known to be above suspicion.

Diphtheria

Factors of prime importance are early recognition of the disease absolute rest and prompt and adequate treatment with antiserum.

Strict isolation must be enforced and all soiled swabs burnt. Complete rest in bed in the recumbent position is desirable for two to three weeks after disappearance of the exudate in hope of preventing or minimising myocardial and neurological lesions. Reading should be limited to at most two hours a day in order to rest the ocular muscles. After this period the patient may be allowed to sit up in bed and a week later he may be carried to a reclining chair. Next a few steps round the room are permitted and in the absence of tachycardia breathlessness or muscular weakness increasing physical activity is allowed. If single cubicles or rooms are not available the patient should be moved to a clean ward after five to six days penicillin treatment to avoid reinfection and the carrier state.

Diet Should be light but nutritious and varied. In severe faucial infections with much concomitant adenitis swallowing may be difficult and thickened milk mixtures ice cream egg flip and jellies are given in frequent small feeds. As in all fevers a high fluid intake must be maintained. During the stage of resolution diet can be rapidly increased provided there is no indication of renal defect.

Specific therapy Antitoxic serum is of signal value in reduction of morbidity and mortality but it must be given early in the course of the infection as diphtheria toxin once fixed in the tissues cannot be neutralised. It is a sound rule that in all cases clinically suggestive of diphtheria 10 000 to 20 000 units of antitoxin should be given at the time of

taking the throat swab. For the clinically or bacteriologically certain case of average severity a dose of 20 000 to 40 000 units should be given into a muscle immediately and repeated in twenty-four hours if definite improvement is not obvious. Severe cases including those showing extensive or poorly consolidated membrane with much faucial oedema, bull neck, laryngeal cases and those seeking advice after thirty-six hours should have the intramuscular dose reinforced by an intravenous one as maximal serum concentration of antibody is not reached until 48 hours after intramuscular injection. It is best to give an adequate dose at the outset and its size must be judged by careful clinical evaluation of the case. A rough guide to antitoxin dosage is to allow 10 000 units for the nose and the same for each tonsil involved and 20 000 units each for pharynx and larynx for each day that the disease has been present. For example 10 000 units will suffice for a primary nasal diphtheria seen on the first day but if the disease involves both tonsils and the larynx and the patient has been ill for forty-eight hours 80 000 units will be the minimum dose and a further 20 000 to 30 000 units should be added if toxæmia is severe. If more than 50 000 units is required one third to half of the dose should be given intravenously. In this case the possibility of anaphylactic reaction must be borne in mind and preliminary test doses of 0.25, 1 and 2 ml injected intravenously at five minute intervals. If no reaction results the full dose is warmed to blood heat and injected slowly through a fine needle. If reaction occurs the remainder of the dose must be given into a muscle. Reactions are controllable by injection of adrenaline 1:1000 5-10 minims subcutaneously and subsequent allergic manifestations such as urticaria respond to antihistamine drugs. If it is necessary to give antitoxin to asthmatics or others in whom sensitivity is known or suspected it is wise to use a preliminary test dose of 5 minims hypodermically. Reaction is an indication for desensitisation by administration of a series of graduated doses subcutaneously commencing with 0.02 ml and ending with 5 ml at ten minute intervals.

In toxic, hemorrhagic and laryngeal cases it is an advantage to add the serum to 100 ml of 10 per cent glucose in

physiological saline and administer by intravenous drip following with 5 per cent glucose saline if required. Intravenous dosage is sometimes impossible in small and weakly children and the serum may be given intraperitoneally (in the mid line just below the umbilicus). Absorption is quicker from this site than from muscle. Age and body weight do not affect the amount of serum required.

Penicillin therapy. Sensitivity of *C. diphtheriae* strains varies widely. Energetic treatment at the outset (2 mega units of crystalline penicillin or 600 000 units of procaine penicillin daily) produces rapid clearance of the infecting organism and secondary invaders from the pharynx. Penicillin V (0.75-1.5 G daily) and erythromycin (1-2.5 G daily) by mouth are also valuable. As the damage in diphtheria is caused by an exotoxin and penicillin cannot be expected to do more than eradicate the infective focus its rôle will therefore be complementary to that of antiserum.

Local treatment. Has definite limitations and its energetic pursuit is to be discouraged. Careful swabbing of the mouth and throat and the provision of simple mouth washes are unobjectionable. When the false membrane begins to disintegrate loose portions may be gently detached with forceps. Electric or hydrostatic suction is valuable for removal of nasal or pharyngeal secretions.

Laryngeal Diphtheria. Associated with high mortality as the victims are usually infants and the respiratory embarrassment induces circulatory exhaustion. In addition to liberal serum therapy the child should be nursed in a steam tent or ward. Where these are not available a tent can be improvised with bed screens or a domestic clothes horse and sheets and the steam introduced from a boiling kettle. Feeding is often difficult and oesophageal intubation may be necessary. Respiratory obstruction should not be allowed to develop and laryngeal intubation or tracheotomy must be resorted to in good time. If the child is being nursed at home tracheotomy is the operation of choice as once the tube has been inserted subsequent management of the case is fairly straightforward. The inner tube should be removed for cleaning at three or four hourly intervals. The disadvantage

of this operation is the subsequent scarring and the possibility of injury to the larynx but the latter can be averted by incising the trachea below the first ring.

In hospital operative interference may often be more tardy and aspiration by direct laryngoscopy may obviate its necessity.

Complications

Cardiac and circulatory weakness should be met by strict recumbency with elevation of the foot of the bed and the use of an oxygen tent. An intravenous saline drip containing noradrenaline is a most useful resource in emergency and hydrocortisone is an excellent supportive measure.

Peripheral neuritis must be watched for and if it occurs rest is provided for the weakened muscles. (See p 288.) Palatal paresis requires careful feeding and liquids should be thickened the use of an œsophageal tube may be necessary. Pharyngeal paresis calls for elevation of the foot of the bed on blocks maintenance of a clear airway by continuous suction of secretions from the pharynx and tube feeding. Atropine hypodermically is helpful. Respiratory paresis is an indication for the use of a mechanical respirator. In paresis of the pharyngeal and respiratory muscles tracheotomy is advantageous in conjunction with the above methods. If a respirator is not available artificial respiration and oxygen inhalation should be tried. Bronchopneumonia is a dangerous complication, and should receive energetic treatment (See p 263.)

Prophylaxis

1 For preference the patient should be treated in an isolation hospital. Isolation is continued until three successive nasal and faucial swabs (taken at intervals of not less than three days and at least two days after cessation of antibiotic therapy) are negative. The nasopharynx should appear healthy and free from discharge. Terminal disinfection of the patient and sickroom is carried out. The disease is notifiable.

2 Contacts should have nasal and throat swabs taken and be Schick tested. They should be quarantined until the results are available and children from an infected house are not

allowed to attend school for twelve days or until shown to be clear. Those giving negative Schick tests and negative swabs are regarded as above suspicion. A negative Schick test and a positive swab is an indication of the carrier state and these should be isolated. Gravis and intermedius strains are regarded as virulent. Antis requires virulence testing. A positive Schick test and negative swab means that these are at risk and should be re-examined and swabbed daily during the epidemic. Where desirable they may be protected by combined passive and active immunisation. Positive Schick test and positive swab indicate clinical diphtheria.

3 Convalescent and healthy carriers of virulent strains should be segregated (and kept separate from acute cases) and given ample dietary tonics, sun and fresh air. Nasopharyngeal abnormalities such as diseased tonsils, adenoids or mastoiditis should be dealt with surgically. Penicillin and erythromycin in liberal dosage are of some value in termination of the carrier state.

4 The present policy of mass immunisation of children has proved conspicuously successful. Immunisation is of most benefit to children between the ages of six months and six years, as in this group natural immunity is lowest and the disease formerly most fatal. Immunisation is therefore advocated for all children at the age of three to eight months.

Purified toxoid adsorbed on aluminium phosphate (P.T.A.P.) gives a Schick conversion rate of over 99 per cent and is the preparation of choice for infant immunisation and for booster dosage of school children and adolescents. Dosage varies according to the preparation employed. Triple antiven (tetanus, pertussis and diphtheria) gives excellent results. Alum precipitated toxoid (A.P.T.) and toxoid anti-toxin floccules (T.A.T.) are now little used. Whatever the prophylactic employed, a full course with proper spacing of the doses is essential. Immunising injections should not be given in the presence of colds, gastro-intestinal upsets or during outbreaks of poliomyelitis.

5 Temporary (passive) immunity is useful in certain circumstances, as in the case of diphtheria contacts who are suffering from some debilitating disease and may be achieved by an intramuscular dose of antitoxin (4 000-8 000 units). It

is unfortunately liable to arouse a false sense of security if there are no contra indications it can be combined with a course of P T A P

Scarlatina

This disease has manifested itself in a comparatively attenuated form during recent years and the anginose malignant and haemorrhagic types are rarely encountered The decision as to home or hospital treatment must depend upon the facilities available

Isolation and nursing are carried out as in other infectious fevers The patient should remain in bed for eight to ten days after desquescence and his return to full activity should be gradual The presence of complications necessitates longer immobilisation

Diet is restricted to fluids and carbohydrates during the febrile phase later in the absence of renal involvement light ordinary diet is allowed If the throat condition makes swallowing difficult semi solids and thickened drinks are most successful

Local and symptomatic treatment Over active local treatment can do harm warm saline or aspirin gargles make for comfort Hot fomentations or kaolin poultices to the neck diminish the pain and trismus associated with cervical adenitis Dover's powder and aspirin alleviate general discomfort and restlessness thus aiding sleep

Specific therapy Because of the mildness of recent epidemics it has not been easy to assess the virtue of scarlatinal antiserum and the introduction of antibiotics has further confused the issue In the light of available information it appears to be a valuable contribution to treatment Anti serum has no effect on established complications but if given early tends to prevent their appearance it effectively combats toxæmia Unnecessary in mild attacks it should be used for severe cases and in debilitated subjects The dose is 16 000-32 000 units When the upper level of dosage is indicated part should be given intravenously with due precaution

Chemotherapy The results of sulphonamide therapy are much in doubt the rash and pyrexia are not materially

Diet Feeding presents a difficult problem in cases where the paroxysms of coughing regularly end in vomiting. Heavy food is undesirable but milk should be given liberally and if fortified will maintain nutrition until the period of stress is over. Custards, milk puddings, eggs, soups and jellies are also useful. Infants should be fed ten to fifteen minutes after an attack; it is an advantage to reduce the bulk of the feeds temporarily, adding glucose or Dextrin maltose. Feeding after paroxysms may be necessary also in older children who vomit copiously in order to prevent serious undernutrition.

Drugs Cough mixtures containing antispasmodics have definite value (ammonium bromide gr. 4, chloral hydrate gr. 2, tincture of belladonna and ammoniated tincture of opium of each 4 minims, chloroform water 10, 1 drachm, four hourly for a child of three years).

Phenobarbitone (gr. $\frac{1}{2}$ twice or thrice daily for a child of one year) will allay apprehension and spasm but cyanosis, bronchopneumonia and pulmonary collapse are contra-indications.

Extensive clinical tests have confirmed the efficacy of chloramphenicol in whooping cough. Dosage is 30-100 mg per kg. body weight daily by six hourly fractional doses. When the spasms are under control the dose may be reduced by half. On account of possible bone marrow toxicity, enthusiasm for chloramphenicol has been partially diverted to oxytetracycline and chlortetracycline seems equally effective. Antibiotics are useless unless given early in the attack.

Specific therapy The use of pertussis vaccine during the catarrhal stage of the disease has its advocates but little benefit is to be expected once spasms appear. Convalescent serum and hyperimmune serum (from adults who have had the disease or who have lately been immunised by vaccine) are not generally available.

Complications

Bronchopneumonia accounts for most of the mortality of whooping cough and should be met by exhibition of penicillin, erythromycin or a cycline antibiotic. Pulmonary collapse is usually associated with bronchopneumonia and

may require postural drainage deep breathing routines and possibly bronchoscopic drainage. Convulsions are best treated by warm baths and administration of a sedative such as soluble butobarbitone 0.075-0.125 G orally. For severe cases withdrawal of cerebrospinal fluid by lumbar puncture oxygen inhalations and an intramuscular injection of amylobarbitone 0.075 G for a child of one year should be tried. Otitis media calls for appropriate attention.

Convalescence

In an average uncomplicated case the child may be allowed up on the fourth or fifth day of the paroxysmal stage and be permitted to play quietly in the fresh air a few days later. Tonics and concentrates of vitamins A and B are of considerable value and a change to the country or seaside will complete convalescence.

Prophylaxis

1 The patient should be isolated for four weeks from the first whoop unless the paroxysms cease and pernasal swabs become negative earlier. Discharges sputa and vomitus are received into wipes or disposable tissues and burnt. The first case in a household is notifiable in some areas.

2 Non immune child contacts should be examined daily for three weeks and be excluded from school. In view of the unreliability of immunity tests it must be assumed that all children who have not had the disease are susceptible. Adult contacts are isolated only if suspicious symptoms develop. Diagnosis during the highly infectious catarrhal stage is important and is facilitated by cough plates or pernasal swabs taken immediately after coughing.

Immunisation Combinations of alum precipitated diphtheria toxoid tetanus toxoid and *H. pertussis* vaccine are available. Three or four monthly intramuscular injections of triple antigen beginning at the fourth month of age induce good temporary immunity to pertussis this can be quickly revived by booster dosage when required.

Meningitis

When a case of meningeal irritation presents the many possible causes must be considered. In meningitis rapidity

blood or plasma transfusion followed by saline to which noradrenaline bitartrate (L-arterenol Levophed Bayer Products) is added (one 4 mg ampoule to 500 ml of normal saline). Cortisone in dosage of 100-200 mg daily by mouth or prednisone in one fifth of this amount is excellent supportive therapy but in critical peripheral circulatory failure hydrocortisone hemisuccinate 100 mg is an intravenous drip is best. Whether corticosteroids are being given or not potassium lack may supervene. Careful watch must be kept on the blood chemistry and hypokalaemia corrected provided that anuria is not present.

Pneumococcal meningitis responds well to combined intrathecal and systemic penicillin but sulphonamide therapy is desirable as a second line of defence.

H. influenzae meningitis varies in its response to chemotherapy and laboratory findings on sensitivity provide a useful indication for treatment. Some can be controlled by penicillin 2-4 mega units daily while other strains are vanquished by streptomycin 0.5 G daily by fractional intramuscular dosage for five to seven days with one or more intrathecal doses of 20-50 mg as required. In general a better response is obtained from chloramphenicol therapy. Prather *et al* confirm its superiority in children with *H. influenzae* and other Gram negative meningeal infections (125-250 mg four hourly for eight to ten days). Sulphadiazine should also be given in all cases.

Meningitis due to *Klebsiella pneumoniae*, *Esch. coli*, *Pseudomonas* and the *Salmonella* group can be treated by a streptomycin sulphadiazine routine although laboratory findings suggest a successful role for neomycin (10-15 mg/kg daily intramuscularly). Polymyxin (2.5 mg/kg daily intramuscularly) is effective against *Pseudomonas* infections.

Staphylococcal meningitis is usually difficult to control and here antibiotic sensitivity varies widely. Pending laboratory indications penicillin 5 to 10 mega units and streptomycin 2 G intramuscularly daily plus penicillin 15 000 units intrathecally is best. If the organism proves penicillin resistant chloramphenicol (0.25 G 4-6-hourly orally until the patient becomes afebrile) with erythromycin 1.2 G orally daily should be tried.

Sterile subdural collections of fluid are a late and trouble some complication of treated meningitis and they are often responsible for recurrent pyrexia and convulsions. Aspiration is usually required.

Tuberculous meningitis Until recently opinion was uniform that combined intramuscular and intrathecal therapy was desirable. It now appears that intramuscular streptomycin with para aminosalicylic acid or isoniazid is equally effective. Streptomycin is given in dosage of 5 mg per kg body weight intramuscularly daily for about eighty days if clinical response has been satisfactory it may then be given on alternate days and later on every fourth day over a total period of about six months. Isoniazid (5-10 mg per kg body weight to a maximum of 300 mg daily by mouth) or para aminosalicylic acid (5-15 G daily by mouth) is given over four to six months.

Relapse may occur even after long periods of good progress but these have been less common where the initial course of therapy has been energetic and not of shorter duration than three months. Somner advised continuation of treatment however favourable the clinical response until the CSF glucose content rises to 50 mg per cent.

Intrathecal tuberculin (P.P.D.) streptokinase heparin and more recently cortisone have been tried with the object of preventing or lessening tuberculous exudate and the risk of spinal block and hydrocephalus. Results have been very variable.

Lymphocytic choriomeningitis A mild meningitic illness due to a virus infection. Vectors are house mice and probably bugs and lice also. The CSF is sterile on culture but shows a marked lymphocytic pleocytosis.

Prophylaxis of Meningococcal Meningitis

1. Hygienic living conditions adequate air space heating and ventilation of dormitories and messrooms.

2. Isolation of patients. The disease is notifiable. Detection of carriers by post nasal swabbing. In small closed communities, mass prophylaxis is by dosage with 4 G sulphadiazine over twenty four hours. This may clear carriers temporarily.

Psittacosis

A virus infection of parrots budgerigars pigeons and hens which is communicable to man. Newly imported birds of the parrot family are very likely to harbour the disease which appears in humans as an influenzal illness with pulmonary consolidation. The tetracyclines are effective (0.5 G orally followed by 250 mg six hourly until deservescence). Chloramphenicol may be used in similar dosage.

Influenza

The many dissimilar diseases grouped under this heading require prompt and energetic treatment as their importance lies mainly in dangerous complications and sequelæ.

It is wise to insist upon complete rest in bed until the temperature has been normal for three days and the patient is free from complications.

For mild cases a light diet with ample fluids an aperient and a few doses of Compound Codeine Tablets B.P. may be all that is required further treatment is symptomatic on lines described for the common cold (p. 252). In more severe cases sulphonamides are usually given sulphadiazine sulphadimidine and sulphasurazole are all suitable. These have no effect on the virus infection but may help to forestall or ameliorate complications caused by the activity of bacterial invaders.

The irritating cough of influenzal tracheitis can be lessened by steam inhalations containing some aromatic substance such as Friars' balsam and a few doses of Codeine Linctus B.P.C. The gastro-intestinal manifestations are often distressing here fluid diet chalk and opium mixture and warmth to the abdomen are helpful but for obstinate diarrhœa one of the little absorbed sulphonamides may be given trial.

Bronchopneumonia is a common and dangerous complication and calls for efficient treatment (see p. 263). Tonsillitis and sinusitis must be treated *secundum artem*.

Myocardial weakness sometimes complicates a severe or neglected attack of influenza. Neuro-circulatory asthenia may occur in predisposed subjects and all shades of psychi-

atric defect may be uncovered. Such troublesome sequelæ can often be avoided by securing adequate convalescence for the patient. Tonics play a minor role but iron and strychnine mixtures and vitamin preparations are often ordered for the asthenic sequelæ.

Prophylaxis

1 Sufferers should be encouraged to remain solitary in the early stages of the attack. The use of disposable tissues and separate tableware and towels should be encouraged.

2 During epidemics avoidance of crowded gatherings, abundance of exercise in the fresh air, correction of unhealthy oronasal conditions. Disinfection of the air in theatres etc with aerosol sprays of hypochlorite or propylene glycol or by U V radiation.

3 Specific Immunisation with appropriate endemic virus strains has given promising results. American figures suggest that 75 per cent of those inoculated escape attack. The antibody response following infection or following inoculation wanes after two months so that repeated dosage at yearly intervals is probably adequate. Inoculation during an epidemic is useless. one valuable activity of W H O is the prediction of outbreaks.

Poliomyelitis

The aim of treatment is to minimise the effects of muscular paralysis. Early diagnosis is a matter of great difficulty in many cases as mild subclinical infections are common. The possibility of poliomyelitis should be considered in all cases of unexplained pyrexia particularly when the disease is prevalent and all short term febrile illnesses treated by total rest. There is good evidence that muscular fatigue or trauma during the invasive stage aggravates the paralysis.

The patient should be isolated and given complete rest. A firm mattress support is necessary to prevent sagging of the spine which would be disastrous if the trunk muscles should become affected. The bed should be equipped with a foot board. Diet suitable to the febrile state is given, and ample fluids allowed. Lumbar puncture should be done as a diagnostic aid and to lessen meningeal irritation. Headache and

muscle pains are relieved by aspirin or its combinations with codeine or Dover's powder but restlessness and insomnia may require phenobarbitone. Retention of urine sometimes occurs and should be relieved by catheterisation. Apart from symptomatic indications drugs have no influence on the course of the disease. Convalescent serum had a short vogue but its value has never been demonstrated.

In the pre paralytic stage painful and tender limbs should *be made comfortable by the use of bed cages, pillows and sandbags*. The application of heat as by radiant heat baths, hot packs or stupes makes for comfort and mental tranquillity. Many cases stop short of paralysis but this manifestation must be sought for and treated with promptitude. Weakened muscles should be supported by splinting the limb in a position of physiological rest to prevent overstretching and deformity. Splintage should be light and easily removable and may be made of Plaster of Paris or Perspex. A plaster shell or bed is necessary where muscles of the trunk or buttock are weakened.

Involvement of the bulbar nuclei is a serious manifestation and its care makes most exacting demands on the skill and patience of the nursing and medical personnel. Accumulation of pharyngeal secretions leads to pulmonary atelectasis and pneumonia and must be prevented by (1) postural drainage (a 30-50° angle of elevation of the trunk and lower limbs but 20° will suffice if the patient can be nursed in the lateral and/or prone positions) (2) continuous suction (3) feeding by pernasal gastric tube (4) oxygen by mask (4-8 litres per minute) (5) mechanical respirator. If a clear airway cannot be maintained by these measures high tracheotomy may prove life saving. A simple closed circuit oxygen inhaler which incorporates soda lime absorption should be available for bulbar cases showing defective deglutition and cough reflex and *pooling of pharyngeal secretions in conjunction* with items 1-4 above. Respiration is assisted by rhythmic compression of the rubber bag. A cuffed rubber tube is passed through a tracheotomy incision thereby closing off the hypopharynx. The tank respirator is reserved for cases of spinal type respiratory paresis. All forms of mechanical respirator are dangerous unless items 1-3 are put in train.

Bronchopneumonia is liable to supervene and must receive treatment by penicillin or broad spectrum antibiotic

Active physiotherapy ought to be introduced just as soon as the stage of muscular tenderness has passed. The application of heat is continued with in order to maintain good peripheral circulation. Limbs that are allowed to become cold and clammy rarely regain good function. Hot stupes, limb baths, radiant heat and short wave diathermy are helpful. Light massage is beneficial and passive movements of the joints of the affected region should be made daily to prevent stiffness and contracture. After a few days the position as regards paralysis usually becomes stabilised and more ambitious physiotherapeutic measures can be employed. Good food, sunlight and fresh air are powerful stimuli to recovery and boredom must be prevented by the provision of suitable bed recreations. It is wise to secure the co-operation of an orthopaedic surgeon from the outset and the services of a skilled and enthusiastic physiotherapist are invaluable.

The electrical reactions of the muscles should be tested and charted from time to time. This provides a useful guide to treatment as attention is directed particularly to those which show signs of recovery and effort not wasted on those hopelessly paralysed. Good circulatory and muscle tone must be striven for and this is incompatible with prolonged immobilisation in splints. These are removed daily and after preliminary heating and massaging of the affected limbs a full range of passive movements should be carried out. The patient can without detriment be encouraged to assist with these movements. The limb is supported so as to counteract the effect of gravity and active contraction of the weakened muscle groups performed.

At this stage help may be given in the form of jointed splints supported from a frame or beam and arranged with pulleys and counterweights or springs wherein the patient can exercise the affected muscles without fatigue. Later progressive exercises against gravity are introduced and finally movements against resistance. Progress should be gradual as overstretching or tiring of the weakened muscles depresses morale and hinders recovery. Many movements which are difficult or impossible in bed are facilitated by the

buoyancy of water and the use of an immersion pool or bath is of great service in the reablement of poliomyelitis victims

The duration of bed rest depends on the circumstances of each case most patients can be allowed up after two to three months The supporting apparatus must be modified or replaced periodically according to progress and the amount of exertion permitted Physiotherapeutic and re-educative measures may be necessary for up to two years suitable orthopaedic appliances will enable the patient to take exercise and regain ordinary activities The rationale of each item of treatment should be explained to the patient as in this affliction intelligent co-operation and self help are important factors in recovery Where feasible a stay at a polio reablement centre is of great benefit to the individual sufferer Orthopaedic treatment e.g. tenotomy tendon transplantation arthrodesis may be of service in correcting residual deformity and improving function

Prophylaxis

1 Isolation of patient and suspects (one week or duration of fever if longer) sterilisation of tableware and bed linen Destruction of swabs and nasal discharges by burning disinfection of faeces as in enteric fever

2 Notification Quarantine of child contacts (three weeks) School closure is of doubtful advantage as it may disperse potential foci of infection and increase the communal hazard on the other hand the individual scholar is safer at home than in an infected school and parents are usually given an option in the matter If the school remains open efficient daily medical inspection is a *sine qua non*

3 As the virus is carried by sewage a high standard of personal domestic and community hygiene is desirable as in prophylaxis of enteric fever During epidemic periods crowded assemblies and sports fixtures should be banned likewise bathing in swimming baths ponds and rivers In view of the possible rôle of droplet infection and nasopharyngeal entry of the virus elective oro-pharyngeal surgery should be postponed Prophylactic injections against other diseases (particularly those given intramuscularly) should be temporarily withheld

4 Protective inoculation Extensive field trials by Hammon and others showed that considerable protection is afforded by injection of gamma globulin (7 ml for a child of five years) Passive immunisation is not satisfactory except in special cases such as pregnant mothers and young child contacts Immunisation by attenuated vaccine is therefore a more desirable procedure and formalised vaccine of the Salk type is in extensive use Dosage is 1 ml intramuscularly and repeated after four to six weeks and six to twelve months Little is known as yet regarding booster dosage requirements Ideally all persons at risk should be protected but young people between the ages of six months and national service intake comprise the urgent target Many practical problems of vaccine production remain—for example where the line should be drawn between adequate attenuation (and complete innocuity) and useful antigenicity The live attenuated poliovirus vaccine of Sabin and Koprowski is given orally as separate virus strains Some difficulties in attenuation arise here also spontaneous mutation is another hazard

Encephalitis

Many different viruses including those of poliomyelitis are capable of causing this condition and the clinical findings show wide variation The cerebrospinal fluid may be normal or contain excess protein and globulin with lymphocytic pleocytosis Lumbar puncture may lessen mental excitement or coma During the febrile phase treatment is that of infectious fevers in general Chloramphenicol and the tetracyclines and cortisone appear to be helpful in some cases Hypnotics such as phenobarbitone and cyclobarbitone are indicated for relief of delirium and insomnia Good nursing and careful feeding are of prime importance and the skin, bowel and bladder usually require attention If coma is prolonged or signs of bulbar involvement appear the measures described under poliomyelitis are necessary

If muscular rigidity develops judicious physiotherapy is of value The patient is encouraged to move about and to regain his physical independence Suitable occupational therapy will help to preserve mental and muscular agility Antispasmodic drugs are useful in some cases and they

should be pushed to the limit of individual tolerance. The best are atropine sulphate gr $\frac{1}{4}$ twice daily by mouth and hyoscine hydrobromide gr $\frac{1}{8}$ twice to thrice daily. Tincture of stramonium in $\frac{1}{2}$ 2 drachm doses is preferred by some patients (see p. 310). Depressive and narcoleptic states and oculogyric crises are improved by amphetamine, one to two tablets of 5 mg. being given each morning. Sufferers showing abnormal behaviour patterns often benefit from the re-education technique of Bond and Appel. Patients with serious antisocial tendencies need institutional care and psychotherapy. Epidemic encephalitis is notifiable. Case to case infection is rare and diagnosis in sporadic instances is often tardy. Isolation is therefore pointless except in epidemic conditions.

Post vaccinal encephalitis and that complicating infectious fevers e.g. measles, mumps and glandular fever respond to general measures outlined above. There is no specific treatment and the use of immune serum has been abandoned.

Morbili Measles

Measles is one of the major scourges of child life on account of the invalidism and mortality associated with its complications and sequelæ. It is moreover a disease which is often regarded with astonishing complacency by otherwise intelligent parents.

Prompt isolation is desirable and the usual infectious sickroom routine established. The room should be airy and comfortably warm. If photophobia is troublesome the eyes should be protected from bright light for a day or two. A fluid diet and a diaphoretic mixture are suitable for the febrile stage. Conjunctivitis responds to three hourly irrigations with boric lotion andunction of the lid margins with soft paraffin. Laryngitis is treated by prescription of a sedative cough mixture such as Codeine Mixture for Infants. B.P.C. and moistening the atmosphere by steam from a bronchitis kettle. An effective steam tent may be improvised with ward screens. The steam valve and the electrically-operated steamer both have the advantage of producing steam without appreciable heat. The possibility of laryngitis in measles being diphtheritic must be borne in mind.

Bronchitis and bronchopneumonia are frequent complications especially in debilitated children and should be treated as described elsewhere. There is some evidence that routine administration of sulphonamides or penicillin in all but the mildst cases will reduce the incidence of inflammatory complications. Convulsions may herald the early febrile phase or later the onset of encephalitis. Treatment is by sedation e.g. Chloral and Potassium Bromide Mixture for infants B.P.C. phenobarbitone gr $\frac{1}{2}$ or butobarbitone gr 1 twice daily for a child of six years. Vomiting and diarrhoea may arise at any stage especially in infants and lead to profound dehydration and shock. Mouth feeding should be limited to sterile water for twelve hours and intravenous fluids (including plasma) given. Otitis media should be watched for and appropriate treatment instituted. Stomatitis responds to gentle cleansing with sodium bicarbonate solution painting ulcerated areas with 0.5 per cent aqueous gentian violet. Citrus juice reinforced with ascorbic acid is helpful in all mouth lesions. Tetona and cancerum oris formerly fatal manifestations are amenable to large doses of penicillin or a broad spectrum antibiotic.

Prolonged convalescence is desirable after measles particularly in cases which have shown complications. Fish liver oil and iron tonics are helpful. Fresh air sunshine and if possible a change to the country or seaside will do much to reinvigorate the patient. A predisposition to disease of the chest or naso-pharynx may be excited by measles or a pre-existing tuberculous focus reactivated.

Specific therapy. Convalescent serum is of doubtful value in treatment of the established attack, but has been used to protect susceptible or attenuate the disease in contacts. For temporary passive immunity it must be given within four days from exposure to infection. If given between the fifth and eighth days the attack will be modified and active immunity re-ult which is in most cases the more satisfactory state of affairs. The dose of pooled convalescent serum is 5-10 ml by intramuscular injection. If this remedy is not available 10-20 ml of adult immune serum may be used. This is of considerably lower potency and in addition to the risk of transmitting infective diseases such as hepatitis;

sypilis and malaria infection may occur in the hæmatoma formed at the injection site

Gamma globulin is separated during the fractionation of pooled human sera and is rich in many antibodies including that of measles. It can be concentrated so that small doses are effective. Reactions are very unusual and the globulin may be heated without deterioration of its antibody content thereby obviating the risk of transmitting homologous serum jaundice etc. The dose is 2 ml intramuscularly before the fifth day for protection and after this for attenuation. In the former case the child is protected for almost four weeks.

Prophylaxis

Isolation. Destruction of discharges by burning, disinfection of fomites by chemicals or steam, terminal cleansing of sickroom. **Notification.** (In some areas the first case in each household is notifiable.) **Clinical and domestic considerations** decide the question of hospitalisation. **Quarantine** of susceptible contacts (three weeks). All children who have not suffered from the disease are considered susceptible. School closure is impracticable but susceptibles should be excluded during epidemics. **Passive immunisation.** attenuation.

Rubella : German Measles

This mild exanthem requires little more than isolation and general fever regime. Infective complications such as otitis media sometimes arise and require routine treatment. Encephalitis is a rare complication and should have treatment as described in the relevant section.

The incidence of German measles during the first trimester of pregnancy may cause congenital malformations in the fetus such as cataract, dental anomalies, cardiac lesions, general hypoplasia, deaf mutism and mental defect. Therapeutic abortion has been considered for such cases. Rubella can be transmitted experimentally with considerable regularity and the suggestion has been made that young girls should be given the disease in rubella camps. It is difficult in practice to confine an infective disease in this way.

Epidemic Parotitis Mumps

Isolation and general fever routine should be arranged. The patient should rest in bed for seven days after deservence in uncomplicated cases. Feeding requires considerable ingenuity as trismus is often a feature semi-solid foodstuffs such as porridge, milk puddings, custard puddings, ice cream and jellies are more easily tolerated than liquids. The mouth and tongue are cleaned with a bland preparation such as Thymol Compound Mouthwash B.P.C. 2 drachms to 2 ounces of water after each meal. Kaolin poultices to the neck will relieve pain and an analgesic such as aspirin or Terebin tablet B.D.H. may be ordered in the evening to encourage sleep.

Complications are comparatively rare in children but occasionally troublesome in adults. For orchitis rest in bed and support for the inflamed testis are necessary. A piece of elastoplast attached to the thighs and stretched under the scrotum forms an effective splint. Stilbestrol (5 mg. daily for ten days) has been recommended as a prophylactic against orchitis in adults also gamma globulin from convalescent patients. Decompression of an inflamed testis by incision of the tunica albuginea has yielded disappointing results. Ovaritis should be met by rest in bed, sedatives and warmth to the lower abdomen. Cortisone and prednisone have been given for symptomatic relief in orchitis and ovaritis. Meningo-encephalitis responds to sedatives and repeated lumbar puncture.

Prophylaxis

Isolation until the patient is free of glandular swelling. Observation of susceptible contacts between the twelfth and twenty-eighth days (malaise, pyrexia and inflammation of Stensen's ducts are suggestive). Destruction of oronasal discharges and disinfection of tableware, towels etc.

Infectious Mononucleosis Glandular Fever

Treatment of this condition is mostly symptomatic. Isolation and rest in bed for one week after deservescence is complete should be advised. The enlarged lymph nodes are

rarely painful and as a rule subside quickly. In the anginose types feeding must be arranged so as to cause minimal discomfort. A mouth wash containing boric acid or thymol should be used for the sake of cleanliness. Extensive false membrane may involve the buccal or faucial mucosa and is usually due to infection with Vincent's organisms. A short course of penicillin by injection is effective in anginose types. Sulphonamides and arsphenamine should not be used because of the abnormal hæmopoietic state. Jaundice is frequent in some outbreaks and requires treatment as described elsewhere. Slow convalescence is desirable.

Prophylaxis

Isolation until apyrexia, destruction of oronasal discharges. Glandular fever is of low infectivity and contacts are not quarantined.

Varicella Chicken Pox

Isolation and general management as for other infectious fevers. Diet should be light and include bland fluids. An alkaline diaphoretic mixture is beneficial. Children are prone to scratch the papules and vesicles and thus may induce sepsis and subsequent scarring. The finger nails should be clipped and the arms restrained or the sleeves of the nightwear sewn up. A soothing lotion such as Oily Calamine Lotion B.P.C. with 0.25 per cent phenol may be applied to the rash. Scalp lesions are very liable to contamination by secondary invaders. If they are numerous the hair should be shortened and the vesicles painted with 1 per cent aqueous gentian violet or cetrimide solution. The scabs must be allowed to mature and separate naturally but a warm bath containing chloroxylenol (Dettol) will encourage the latter process.

Cases showing extensive hæmorrhagic or septic rash should have a course of systemic penicillin.

Prophylaxis

Chicken pox is a highly infectious disease. Isolation should be enforced until the primary crusts have separated and the

underlying ulcers are healed. Disinfection of clothing, bed linen and tableware. Susceptible contacts should be excluded from school for twenty six days from exposure. The identity of chicken pox and herpes zoster viruses should be remembered and susceptible children not exposed to the latter. Gamma globulin (2.5 ml. into a muscle) has been used with some success.

Varicella Smallpox

Patients and suspects should be removed to separate wards of a self-contained isolation hospital without delay. Single bed wards are desirable and free ventilation is of utmost importance.

The disease is often a prolonged and exhausting one and everything possible should be done to sustain the patient's strength. Treatment is otherwise directed to minimising skin sepsis and toxæmia which are most disquieting features of severe cases. Diet should be liberal and consist mainly of liquids and semisolids during the pyrexial stage. Persistent vomiting may be troublesome and calls for temporary cessation of feeding and one or two intramuscular doses of chlorpromazine (Largactil M & B) 25-50 mg. Fluid intake must be maintained and in ravenous glucose saline is often necessary.

Where the rash is profuse irritation may be allayed by application of 0.25 per cent. phenol paint. In many cases the skin becomes sodden and tender making the patient a state miserable and some comfort is gained by the application of compresses of cool 1 per cent. potassium permanganate. Seriously ill patients with extensive skin involvement often find dressings of any kind intolerable. In these circumstances the bedding becomes soaked and malodorous. The best remedy is to place the sufferer between sheets of light plastic material so arranged as to drain into a receptacle at the foot of the bed. The skin of the trunk and limbs is then irrigated every two hours with 1:500 potassium permanganate or 1:40 chlorinated soda solution. By this method the patient may be kept clean and comfortable with a minimum of disturbance and if hydrotherapy becomes necessary for reduction of hyperpyrexia its application is simple.

hyperpnoea delirium and coma. The condition can be corrected by reduction of dosage and the administration of glucose and alkalis. Prolonged salicylate therapy depresses prothrombin formation giving rise to purpuric eruptions this is an indication for dosage with vitamin K analogues.

Salicylates have serious rivals in cortisone and prednisone. Disappearance of pyrexia toxæmia and joint inflammation occurs in one to five days in uncomplicated cases and all seem eventually to be controlled by the corticosteroids. It was thought that they might prevent or reverse cardiac damage but further experience has not been completely happy in this regard in some cases cardiac lesions developed during the course of hormone therapy. In the presence of cardiac enlargement or pericardial effusion methylprednisolone (Medrone Upjohn) is preferred as causing least water retention. That the action is suppressive rather than curative is evidenced by the fact that relapse (with signs of cardiac damage) may follow premature cessation of therapy. It is important therefore that modified dosage be continued throughout the natural period of the disease which is six to twelve weeks. No immunity is provided against fresh rheumatic attacks. Dosage cortisone 200 mg on the first day and 100 mg daily thereafter in three to four divided doses prednisolone in one fifth or methylprednisolone in one sixth of this dosage.

The painful joints may be wrapped in warm cotton wool and lightly bandaged but moist heat in the form of alkaline fomentations or kaolin poultices is preferred by some. Local rest and freedom from pressure are secured by the use of bed cage and pillows. Hyperpyrexia is usually a sign of severe cardiac involvement and should be treated by tepid packs or sponging in addition to systemic therapy.

When the acute pyrexial phase has passed a definite scheme for convalescence and rehabilitation must be formulated. It is sometimes difficult to keep young rheumatics in bed once symptoms have subsided but it is desirable if complications are absent to continue the bed rest for four to six weeks. Such ordinary childhood occupations as can be conducted in bed will keep the patient content and in fine weather he may be moved out of doors during the day. Later he may

be carried to a sofa or chair and gradually given the freedom of the room and garden.

Physical exertion should be carefully graduated and its effect judged by regular observations of the sleeping pulse rate and erythrocyte sedimentation rate. A rise in either indicates that further rest is desirable. Increase in body weight is an indication of progress. Needless incarceration does harm and each case must be managed in accordance with condition and progress. In particular careful watch must be kept for evidence of cardiac damage.

All possible aids to convalescence and prevention of relapse should be invoked. Liberal protein rich diet, change of air and tonics are helpful. Hypochromic anaemia is a common finding and should be met by iron medication. Sensible precautions against upper respiratory infections are enjoined. Exposure to damp and cold and the wearing of wet clothing are to be avoided. Sulphonamides and penicillin have no influence on the course of rheumatic fever but are useful for prevention and treatment of β haemolytic streptococcal throat infections which are productive of further rheumatic activity. Phenoxymethylpenicillin (Penicillin V) by mouth offers a convenient and effective prophylaxis. Dosage of 125 mg twice daily may be given almost continuously over a period of five years or until leaving school whichever is the longer (Royal College of Physicians Rheumatic Fever Committee 1957). Monthly intramuscular injections of 600 000 units of benzathine penicillin G may be more suitable for some cases.

Tonsil and adenoid surgery has a disappointingly slight effect on the course of rheumatism but obviously diseased tonsils should be removed when the rheumatic process has become quiescent. A course of penicillin should be given to cover the operative period.

The Public Health aspects of rheumatism are of vital importance. Poor environment, insanitary housing and school accommodation, malnutrition and ignorance of the lady in regard to the seriousness of rheumatic ailments are root causes. Rheumatic fever is notifiable.

Gonorrhoea

The chances of a favourable issue are enhanced if the patient will lead a quiet life avoiding alcohol and excessive

physical exertion during treatment. Sexual intercourse should be proscribed until tests of cure are satisfactory.

Treatment by sulphonamides or penicillin offers an almost certain cure in uncomplicated cases and such treatment may often be ambulant. It should however be adequate otherwise there is risk of the infecting organism becoming resistant. Sulpha resistance is not uncommon but recourse to penicillin therapy will retrieve the situation. The disinfecting action of these drugs is so rapid that it is desirable to take swabs for bacteriological examination before treatment is begun otherwise diagnosis may remain in doubt.

Sulphonamide treatment. The average dosage of sulpha dimidine is 4 G daily in divided four hourly doses for six to eight days. Sulphamerazine is convenient on account of its slow excretion and 1 G at eight hourly intervals will suffice. A reasonable fluid intake should be maintained (about 4 pints daily). If unsuccessful a second course consisting of two-thirds of the amount originally given may be ordered but penicillin would be preferable.

Penicillin treatment. More efficient and acts more rapidly than sulphonamides. It will often clear long-standing relapsed and sulpha resistant cases and is more effective against metastatic complications. A single injection of 300 000 units of procaine penicillin will clear fresh and uncomplicated cases; failures are usually due to reinfection or misdiagnosis (*non specific urethritis does not respond*). Penicillin tends to mask concurrent syphilis even in the small dosage required. Sulphonamides and streptomycin are free from this objection. L. P. Sheil (1956) reports good results from 240 mg of phenoxymethylpenicillin orally thrice daily for three days but many authorities prefer the parenteral method.

Streptomycin treatment. Gonorrhoeal infections respond well and Chinn reported good results from a single intramuscular dose of 0.6 G.

The broad spectrum antibiotics appear to be equally effective therapeutic agents in gonorrhoea. Greaves reports that a single dose of 750 mg chloramphenicol cured 96 per cent of seventy cases and two doses of 0.5 G of oxytetracycline orally with a six hour interval between was similarly

effective in the hands of Wright and his colleagues. The tetracyclines, chloramphenicol and erythromycin have been found useful for resistant and relapsed cases.

The patient should be kept under observation for some weeks or months after apparent cure. Satisfactory tests of cure in the male include a series of negative smears of urethral secretion taken on rising, normal findings on urethroscopy and passage of a urethral sound. Cultures of prostatic secretion after digital massage should be negative for gonococci. In the female, inspection of the urethra, vagina, cervix should show no inflammatory reaction; cultures of swabs from urethra and cervix (post menstrual) should be negative for gonococci. Serological reactions for syphilis should be negative. Lack of complete therapeutic success suggests the presence of an undrained focus of infection and a thorough genito-urinary investigation should be undertaken with provision of suitable drainage.

Local treatment. This is not used as a routine and simple cleanliness is sufficient. Balanitis requires rest in bed, warm baths, gentle irrigation of the sub-preputial sulcus with potassium permanganate (1:5000) and dressing with wipes moistened with proflavine emulsion (1:1000).

For epididymitis rest in bed is indicated and support should be provided by a testicular splint or sling. An evaporating lotion will help to relieve pain and Codeine Compound Tablets B.P.C. are useful. A full course of penicillin is desirable. Seminal vesiculitis and prostatitis are improved by rest in bed and frequent hot baths. Short wave diathermy is of great service and penicillin should be given. If a prostatic abscess develops surgical drainage may be required. Chronic prostatitis usually responds to digital massage via the rectum performed daily for seven to ten days. Bacteriological examination of the expressed secretion should be done and penicillin given by intramuscular injection if the organism is sensitive. For infections with coliform organisms sulphonamide or chloramphenicol may be tried.

There is perhaps more necessity for local treatment in the female. In the early stages nothing more drastic than warm sitz baths is required. When discharge and local irritation have subsided low pressure vaginal douching and urethral

irrigation with 1 : 5 000 potassium permanganate solution may be helpful but these are best entrusted to a nurse. For persistent cervicitis 1 per cent mercurochrome solution should be applied to the cervix vaginal fornices and urethra after preliminary douching and swabbing the vagina dry. This may be repeated at intervals of two to three days. Proctitis should be treated by a short course of twice daily rectal irrigations with 1 : 5 000 acriflavine and insertion of 2 per cent silver proteinate suppositories. Bartholinitis is treated by rest in bed and penicillin injections. Abscess formation is dealt with by aspiration or incision. Removal of the gland by dissection may be necessary later. Salpingitis calls for rest in the Fowler position, warmth to the lower abdomen and sedatives as required. Penicillin should be given in full dosage.

Conjunctivitis can be avoided by teaching patients the hygiene of washing the hands. When this complication arises care must be taken to avoid infecting the sound eye although this risk has diminished with the introduction of antibiotic treatment. Purulent discharge should be removed by irrigating the conjunctiva with warm normal saline three hourly followed by the instillation of Penicillin Eye drops. B.P.C. Systemic penicillin or tetracycline therapy is also of value. Atropine should be used to keep the pupil dilated.

Arthritis calls for confinement to bed for ten to fourteen days after inflammation has settled down. The limb should be steadied by the use of sandbags or a light splint and heat applied to the affected joints. A seven to twelve days course of penicillin is usually curative. Purulent joint effusions should be replaced by 10 000 to 20 000 units of penicillin in saline using strict aseptic technique. Septicæmia usually responds to heavy dosage with penicillin (2-4 mega units daily by three hourly injection with or without streptomycin 1 G daily). Repeated blood cultures should be done to check progress and change made to tetracycline or chloramphenicol if necessary.

Prophylaxis

Ambulant isolation for the patient including separate towels, clothing, tableware etc. Disinfection of bath and

wash basin after use burning of soiled dressings The wearing of an improvised gonorrhoea bag or in females of sanitary pads will prevent unnecessary soiling of clothing Tactful search for contacts and source Parturient women suspected of harbouring *N. gonorrhoeae* should receive 200 000 units of crystalline penicillin and 300 000-600 000 units of procaine penicillin to prevent ophthalmia in the infant

Reiter's syndrome Characterised by polyarthritides urethritis skin lesions and conjunctivitis Onset may be acute the urethro-balanitis being an early symptom The discharge never contains gonococci Chronic and relapsing varieties have been described Tetracyclines gold and cortisone have all been reported suppressive

Syphilis

Prompt diagnosis is a prerequisite for successful treatment and this can often be made by dark field examination of serum expressed from chancres or from gland puncture while serological tests are still uninformative Single serological tests may be fallacious as may be a purely clinical diagnosis hence the desirability of quantitative and confirmative tests (including treponema immobilisation) Management of the case includes careful observation and treatment of regular sexual and domestic contacts

Penicillin has of late years ousted the arsenicals for routine treatment of syphilis and the combined courses formerly popular have disappeared from most clinics

Primary and secondary syphilis Penicillin is the treatment of choice All types of benzylpenicillin are effective but one or other of the following may be used according to circumstances

1 Procaine penicillin in oil with aluminium monostearate (P.A.M.) 1 200 000 units intramuscularly daily for 10 days followed by 600 000 units twice weekly for six weeks or Bismuth Injection B.P. 1 ml intramuscularly weekly for ten weeks

2 Crystalline penicillin 2 mega units intramuscularly daily by three hourly divided doses for six days followed by P.A.M. 600 000 units twice weekly or Bismuth Injection as above

The patient should be carefully examined and serological tests done every two months for six months and then every three months for two years. The C S F should be examined at one and two years. Relapsed or reinfectd cases should have a repeat course.

For early or late infections involving vital tissues where Herxheimer or paradoxical reactions would be undesirable the above mentioned courses should be preceded by potassium iodide mixture (gr 10-20 thrice daily) and Bismuth Injection B P 0.5 ml intramuscularly weekly for four weeks. Allergic manifestations (urticaria, facial oedema, joint swelling) may complicate penicillin therapy. These respond to antihistamines. Herxheimer reactions typically following therapy of infectious syphilis have as general manifestations collapse, pyrexia, leucocytosis. Local implications consist of temporary aggravation of syphilitic lesions in heart, liver, brain, etc. Immediate treatment is rest, antihistamines and if severe, cortisone. Dosage schedules should be reduced. Allergic reactions may be due to penicillin sensitivity and skin disturbance is the commonest. A broad spectrum antibiotic (tetracycline, chloramphenicol) should be substituted in dosage of 20 mg per kg body weight daily for eight days.

Latent syphilis. Treated by a course of ten daily injections of 600 000 units of procaine penicillin in oil with aluminium monostearate (P A M) followed by Bismuth Injection B P 1 ml intramuscularly twice weekly for ten weeks.

Follow up consists of serological examinations at three monthly intervals for one year, then yearly C S F examination at three months and one year. Any serological relapse calls for re-treatment. Many old latent cases are sero-resistant.

Cardiovascular syphilis. Cardiac failure should be corrected as far as possible before embarking on specific therapy. Young and middle aged subjects with active aortic lesions should have fourteen days potassium iodide (gr 10-20 thrice daily) with four doses of 0.5 ml of Bismuth Injection B P followed by a ten days course of P A M (600 000 units daily) or crystalline penicillin 1 mega unit daily by three-hourly injections for ten days.

Neurosyphilis. Meningovascular manifestations appear relatively early and are usually responsive to therapy, whereas

parenchymatous lesions (tabes and general paralysis) are less amenable. The following routine is applicable to all types.

Procaine penicillin in oil with aluminum monostearate (P A M) 600 000 units intramuscularly daily for fourteen doses. Reactions of the Herxheimer type are dangerous in neurosyphilis. It is doubtful whether any previous medication (iodide mercury bismuth) will reduce this risk.

Serological tests are not helpful in judging progress. Clinical improvement is heartening but unreliable and improvement in the C.S.F. findings is the only valuable criterion of cure. C.S.F. examinations are done before and on conclusion of treatment at three months and then annually for five years. Signs of relapse are an indication for re-treatment.

General paresis requires one or more penicillin courses according to laboratory findings. General health and nutrition should be attended to and obesity if present, corrected. Those with severe psychotic tendencies require institutional care until the effect of specific therapy can be gauged. Penicillin may temporarily aggravate the mental disturbance.

Tabes dorsalis. Penicillin treatment as described for meningo-vascular syphilis. Serological and C.S.F. findings are not always helpful in tabes and several penicillin courses may be necessary to halt the disease process. Attention to the general health and avoidance of all excess is desirable. Unnecessary confinement to bed is harmful and reasonable activity beneficial. Physiotherapy in the form of massage and re-educational exercises will improve muscle tone and co-ordination and restore self-confidence. The patient should empty the urinary bladder at three hourly intervals by day. Retention requires catheterisation with the usual precautions against sepsis. Frank urinary infection should be treated by appropriate bacteriostatics. Lightning pains are often most resistant to treatment. Analgesics like Codeine Compound Tablets should be tried and Panadol (aceto aminophenol) Bayer is very effective in some cases. Pentobarbitone sodium gr 1½ with codeine phosphate gr ½ is useful at night when pains disturb sleep. Morphine is undesirable on account of addictability but pethidine or Pethidorfan Roche 50-100 mg. is perhaps safer for occasional use. Inhalation of amyl nitrite is useful against laryngeal crises. rectal crises yield to hot enemata and morphine suppositories.

(4 G) Large intake of Vitamin B concentrates will some times lessen the frequency of these painful manifestations

Comfortable shoes and well fitted socks are desirable for prevention of perforating ulcers. The feet should be kept clean and dry and amateur chiropody interdicted. If an ulcer develops it should be curetted and packed with soft paraffin tulle dressing. Arthropathies show scant improvement with any therapy but effusions should be aspirated. For disorganised knee joint orthopedic possibilities (including arthrodesis) should be considered.

Primary optic atrophy If the pre treatment vision is 6/20 or better arrest of the process is likely. Martin (1955) recommends a mercurial injection potassium iodide and penicillin sequence.

Congenital syphilis Early recognition and treatment are of vital importance. The minimum daily penicillin dosage for children is 10 000-20 000 units per lb body weight. Three hourly injections of crystalline penicillin are preferred for infants either this or P A will serve for older children. In cases of ocular involvement the assistance of an oculist should be secured as atropine and cortisone locally are often necessary.

Physical examination and serological tests should be done monthly for six months and subsequently every six months for two years. C S F examination on conclusion of treatment. Relapse should be met by further penicillin courses.

Syphilis and marriage For early infective cases marriage is interdicted for two years. serological and C S F findings should be consistently negative by this time. Early latent sero-fast cases who are clinically normal and who have normal C S F findings may marry but should avoid issue for two years. Late latent cases may marry after satisfactory treatment. Cardiac or neurological involvement should be a bar to marriage.

The non infected partner must be made aware of the facts.

Syphilis and pregnancy A patient who has had ample treatment and consistently satisfactory laboratory reports afterwards probably requires no further therapy but regular serological tests should be undertaken to detect reactivation. Present day therapeutic routines are so safe that there is much

to be used for treatment of all pregnant women who have been infected. For cases previously satisfactorily cured for ten injections each of 600 000 units of P A M over a period of four weeks is adequate. For cases first coming to treatment during pregnancy either of the schedules described for primary syphilis should be used. Clinical and serological follow up monthly until confinement. CSF examination may be postponed until after confinement.

Chancroid Soft Sore

Syphilis should be excluded by serological and microscopic tests. Soft sore responds quickly to sulphonamides and to almost all antibiotics. Chlorotetracycline is particularly effective (750 mg. twelve hourly for three days). Local treatment consists of thrice-daily irrigation of the coronal sulcus with 1% 0.05 permanganate solution and application of proflavine solution.

Leptospirosis Ictero-haemorrhagica Weil's Disease

Diagnosis is often difficult and mild cases may be anicteric throughout. The possibility of contact with rat excreta should be explored in unexplained pyrexia in farm workers, veterinarians and persons whose occupation involves handling fish or meat. Canicola fever caused by infection with *L. canicola* is transmitted by contact with urine of dogs suffering from the infection. Pigs are carriers in some countries.

In the icteric stage differentiation from other causes of febrile jaundice is facilitated by the fact that with the exception of septic cholangitis these are the only icteric illnesses showing polymorph leucocytes.

Treatment is most successful in the pre-icteric stage. In cases allowed to progress to severe renal and hepatic damage the outlook is grave. Penicillin in dosage of 2-4 mega units daily if given early appears to shorten the course of the disease although its efficacy is not uniform. Reports of successful treatment by the tetracyclines have been noted Hall and his co-workers concluded that five antibiotics tested had no appreciable effect on the infection whereas Down and Mackay Dick have recently reported satisfactory results from penicillin. In a sporadic disease of this kind

dosage of 70-100 mg per stone body weight as a 1 per cent solution by intravenous drip or as Tolseram 8.24 G daily as 2 per cent solution in saline with 25 mg thiamine and 100 mg ascorbic acid Succinylcholine is a flexible and more rapid relaxant than curarin gallamine or mephenesin which is administered by intravenous infusion in decreasing dosage of from 2.5 to 0.2 mg per minute according to muscular tone and tolerance

Chlorpromazine (Largactil M & II) appears useful as an extender of the sedatives and relaxants employed. Adrian and Kerr combined this drug with barbiturates and mephenesin. The intravenous dose is 15-40 mg six to eight hourly.

Respiratory embarrassment may arise in cases under the influence of barbiturates and muscle relaxants for this reason a closed-circuit oxygen inhaler and bronchoscopic drainage should be constantly available. Tracheotomy (under local anaesthesia) is a life-saving measure in presence of prolonged spasm of the respiratory muscles laryngeal or bronchial obstruction by retained secretions or coma. It should be done early rather than as a desperate resort.

The help of a skilled anaesthetist is invaluable in the management of a case of tetanus.

Surgical treatment. Extensive operations such as amputation should be postponed until the general condition improves and some degree of immunity has accrued. If the wound is unhealed it should not be dealt with until one hour after the injection of antiserum. Necrotic tissue debris and foreign bodies should be removed. Sinuses are opened up or excised and free drainage provided. Traumatization of non-infected tissues is to be avoided otherwise absorption of toxin is facilitated. The wound may be irrigated with antitoxin but some authorities prefer hydrogen peroxide. In the case of limb lesions rest is secured by splintage.

If spasm of the paravertebral musculature has been a prominent feature radiographs of the spine should be obtained before the patient is allowed up to exclude fracture.

Prophylaxis

Careful sterilization of surgical dressings ligatures and sulphonamide powder used for dusting wounds. Antiseptic

treatment of wounds and abrasions soiled with road dust or earth. Irregular and lacerated wounds should be excised aseptically or subjected to *debridement* if excision is impracticable. Antitoxin should be given prophylactically if the risk of tetanus exists a most difficult decision as in some cases the injury is so trivial as to pass unnoticed. dose 5 000 10 000 units intramuscularly and repeat after eleven days if required or before further surgical interference. In subjects who have been immunised with formol toxoid a booster dose of 1 ml is probably an adequate safeguard unless the wound is of the deep penetrating type which cannot be quickly cleaned surgically. In this case antitoxin should be given as well. Within ten years of immunisation the boost begins inside four days.

Active immunisation with formol toxoid has proved of great value and its use in the community generally would be desirable. It is given in 1 ml doses subcutaneously on three occasions at intervals of six weeks followed by booster doses at five yearly intervals. The dose for infants is 0.5 ml. Useful immunity accrues ten days after the second injection. (See p. 26.)

Anthrax

Sevlav's serum is used in dosage of 100-200 ml intravenously daily for five days. Anaphylactic reactions are common. Favourable results have been reported from sulphonamide treatment but penicillin seems to be the most effective mode of therapy. It should be given in liberal amounts i.e. 1 mega unit followed by 250 000 units six hourly for eight days combined with oral sulphadiazine. Clarke found chlortetracycline effective in cutaneous anthrax. His routine is 60 mg per kg body weight divided into four doses which are given at hourly intervals then 26 mg. per kg thrice daily for two days and the dose gradually reduced over the next four days.

Surgical treatment of superficial lesions is not advised. rest, splintage and simple dressings are sufficient.

Prophylaxis

Immunisation of susceptible animals with purified antigen of B. lion and Strange. Incineration or deep burial of animals

dying of anthrax Disinfection of hides wool hair and bristle before processing and the elimination of dust from work shops Care in handling bone meal and other imported feeding stuffs Notification

Actinomycosis

These infections are chronic in nature and variable in response to treatment with tendency to relapse The following remedies should be tried alternately or in combination and for relatively prolonged periods

Iodides A traditional remedy by reason of their reputed absorptive action on granulomatous tissue Dosage should be about gr 60-90 thrice daily for three to four weeks

Sulphonamides Sulphadiazine in dosage of 1 G four hourly for four weeks is a useful adjuvant to antibiotics

Penicillin Some pathogenic strains of Actinomyces are sensitive to this drug and dosage of 2-4 mega units daily over one to two months is often effective

Streptomycin Helpful in some cases but dosage must be liberal (2 G sulphate intramuscularly daily for one month followed by 1 G daily in the second and perhaps third months) In intestinal infections it is customary to give half the daily dose by mouth

Oxytetracycline Has proved more consistently successful than the other broad spectrum antibiotics Give 500 mg orally six hourly over two to six weeks

Isoniazid has been found useful as an adjuvant

Surgical treatment. Purulent pleural and peritoneal exudates should be drained and abscesses incised Oseous infections require more radical measures once effective chemotherapy has been established Pulmonary intestinal and renal lesions without fistulation may sometimes be removed completely which results in rapid general improvement

Radiotherapy Sometimes of value in conjunction with other lines of treatment

Infective Hepatitis

This is the commonest cause of jaundice During epidemics many anicteric and sub-clinical cases arise It is

probably due to virus infection and has been transmitted experimentally by serum faeces and urine of infected persons. Outbreaks are prone to occur in schools and are a cause of substantial man power wastage among troops on active service.

Treatment is largely symptomatic. Rest in bed should be insisted upon until the temperature is normal and the skin free from jaundice. Nausea and vomiting interfere with appetite and skimmed milk and bland fluids are sufficient for the first few days. As soon as the fever jaundice and anorexia abate diet should be increased especially with regard to carbohydrate and protein content. A moderate allowance of fat is harmless once appetite has returned. A liberal fluid intake must be maintained throughout the illness if poorly tolerated by mouth intravenous glucose (5-10 per cent) infusions should be resorted to. Aperients are used sparingly as their injudicious consumption probably increases hepatic damage.

Cortisone and allied corticosteroids are of some value in cases of infective hepatitis which are slow to clear.

Convalescent patients should not be allowed to resume ordinary diet and activities until the liver has returned to its normal size and they are advised to abstain from alcohol for two years. They are permanently unacceptable as blood donors.

Homologous serum jaundice. An unpleasant side effect of blood serum or plasma injections. Syringe jaundice may complicate the administration of arsenicals gold etc. or the taking of blood specimens by venepuncture. In the case of serum jaundice the blood convalescent serum or pooled plasma has become infected with the icterogenic agent. In syringe jaundice the syringe or needle has been contaminated and adequate sterilisation of these between cases will prevent the disease. Infective hepatitis and serum hepatitis viruses do not induce reciprocal immunity and are presumed to be distinct. The former is infective on inoculation and ingestion and is present in the blood faeces and urine whereas the latter is transmissible by inoculation and is found in the blood. Gamma globulin gives doubtful protection against serum hepatitis (which does not give rise to epidemics).

Prophylaxis

Gamma globulin one intramuscular injection of 0.3 ml per kg body weight. Strict cleanliness in the handling of food in kitchens and dining halls. Crockery and cutlery should be washed in hot detergent solution then rinsed in hot 0.1 per cent bleaching powder solution which is allowed to dry on. Anti fly measures. Careful cleansing of syringes and needles after use. All glass syringes are best as they can be sterilised in the hot oven at 160 °C for one hour without damage.

Notification

Efforts have been made (by a combination of exposure to ultra violet light and addition of β propiolactone) to inactivate plasma of I H virus.

CHAPTER III

INTESTINAL PARASITES

Ascariasis

Infestation with *Ascaris lumbricoides* is world wide and children are particularly prone. Owing to the wandering propensities of this parasite ascariasis pneumonia obstructive appendicitis or hepatitis may occur.

Treatment. Piperazine is the most effective remedy. For adults a single dose of 3.5 G of the citrate usually suffices for a child of 30-60 lb 2.25 G and for one of 15-30 lb 1.15 G. Santonin is a traditional treatment for an adult gr 3.5 and for a child gr $\frac{1}{2}$ -2 is given with calomel at bedtime and followed by a morning saline. Hexylresorcinol is used in capsule form in dosage of gr 1 $\frac{1}{2}$ for each year of age with a maximum of gr 15 for an adult. A saline aperient should be given on the evening before treatment and the patient goes to bed supperless. The dose is taken on waking and followed by a saline in two hours. Food may be allowed after four hours and the routine repeated in five days. Oil of chenopodium is efficient against round worms but less toxic remedies are preferable.

Prevention. Attention to personal hygiene and avoidance of uncooked vegetables and other foodstuffs.

Oxyuriasis Enterobiasis

Threadworms inhabit the large bowel from caecum to rectum. Eggs are not normally found in the faeces as the female emerges from the rectum to oviposit. Ova may be found on the skin of the perineal region by use of a cellophane or better a Sellotape swab. Scratching causes transference of ova to the nail beds thence to the nose and mouth.

Treatment. *Gentian violet* *Piperazine*. Clinical trials have shown that piperazine hydrate and gentian violet produced

clearance in 90 and 70 per cent of cases respectively. Piperazine hydrate (Antepar elvir ■ W) is used in dosage of 50-75 mg per kg body weight daily for two weekly courses with an interval of one week. No toxic effects are encountered with this dosage. Gentian violet ■ used as enteric-coated capsules in dosage of gr 1 thrice daily for ten days and repeated after an interval of one week (adult). For children the dose is gr $\frac{1}{2}$ per year of age daily given in divided doses for eight days. A second course should follow a rest of seven days. Dithiazanine "Telmid" Lilly is effective in dosage of one 100 mg tablet thrice daily (under 10 years twice daily) for five days.

Oxytetracycline The daily dose is 10 mg per lb body weight in three divided doses for seven days. The drug probably has a direct action on the mature gravid female parasite but is expensive for treatment of whole households.

Enemata Quassia and saline enemata are not effective alone as they clear the lower bowel only. After a preliminary saline wash 6-8 oz. of quassia infusion or hexylresorcinol solution (1 : 2 000) is injected slowly and retained.

Prophylaxis

Keep the nails short and the hands clean. Beds should not be shared. Bath tubs are thought to spread the infestation; standing up showers are preferable. Soak night clothes in ammonia solution or boil before laundering. Sleeping drawers and gloves should be worn at night to prevent scratching. The perineal region is smeared at night with ammoniated mercury ointment. It is essential to treat other carriers in the household e.g. siblings and mother.

Trichiniasis

Acquired by eating improperly cooked pork usually sausage meat which is infested with larvæ of *Trichinella spiralis*. Trichiniasis occurs as a natural infestation in rats and is maintained by their habit of cannibalism. Pigs are infected by eating dead rats or garbage containing infected pork. This cycle must be broken in order to control an outbreak of the disease.

The clinical manifestations are variable. If only a few larvæ are ingested, no symptoms arise. Massive dosage produces an illness resembling food poisoning. Later muscle pains, C.N.S. disturbance, hiccough and difficulty in breathing occur and bronchopneumonia may prove fatal. Facial oedema, splinter shaped hemorrhages under the nails and eosinophilia are characteristic.

Treatment. There is no specific remedy. In the early stage give one ounce of castor oil and follow with a saline purgative in one hour. Tetrachlorethylene may be used in the early stages to get rid of as many adult worms as possible. In the later stages treatment is symptomatic. Cortisone may prove useful. Eosinophilia slowly subsides and there is a progressive rise in antibodies after this treatment.

Control of outbreaks of trichiniasis. 1. Suspect trichiniasis if members of a household become suddenly ill after eating pork products and inform the Sanitary Authority.

2. Collect samples of the patient's faeces and blood and of suspected pork for laboratory examination.

Discourage the consumption of pork unless thoroughly cooked. Freezing at -35° for five minutes renders it safe.

3. Institute inspection of pork. Carcasses of pigs found dead should be burnt.

4. Adequate disposal of garbage. Compulsory corking of swill fed to pigs.

5. Introduce an efficient anti-rat campaign. (See p. 358.)

Teniasis

The tapeworm inhabits the small intestine. Occasionally the cysticercus stage occurs in man, producing serious results such as cysticercosis due to *Tenia solium* and echinococcal cysts due to *Tenia echinococcus*.

Drugs used in treatment. Male fern, Mepacrine, Dichlorophen.

Extract of Male Fern. B.P. (*Aspidium oleoresin*). Administered in mucilaginous suspensions or in capsules in three equal doses of 15-30 minims at intervals of half an hour. Children are given 1 minim per year of age for three doses. Castor oil should not be used in association with this drug.

Mepacrine. The routine is days 1, 2. Sodium sulphate

60 ml. of saturated solution morning and evening Fluids only with glucose Sodium bicarbonate 2 G in water thrice daily day 3 6 a.m. Mepacrine 1 G (ten tablets for adults) washed down with sodium bicarbonate 2 G in a glass of water The patient stays in bed and sips water only until the bowels move 9 a.m. If no scolex visible give a soap enema 10 a.m. (or when scolex passed) breakfast

Dichlorophen (Antiphen M & B) Differs from other tennifuges in exerting a direct lethal effect upon the worms which are killed and digested so that on passage the parasite is macerated and unrecognisable No purging or starvation required may be given as a single morning dose of one tablet (0.5 G) per 16 lb (7.25 kg) body weight to maximum of 6 G or 2 G twelve hourly for three doses (adults)

These remedies have replaced male fern

Cysticercosis Focal epilepsy and intracranial compression in Europeans returned from the tropics are sometimes caused by cerebral lodgement of the parasites Treatment is as for epilepsy Decompression and removal of accessible cysts is feasible in some cases

Hydatid cysts Principal sites are the liver and lungs but they may localise anywhere Jacksonian epilepsy may occur and should have symptomatic treatment Surgical treatment may be attempted in suitable cases Aspiration of the cyst is unwise as the fluid is toxic and severe anaphylactic reaction is likely to result It must be removed intact if possible if not it should be marsupialised and allowed to fill with granulation tissue

Prevention of tapeworm disease Inspection of slaughter houses and meat to detect cysticerci Attention to personal hygiene particularly in relation to dogs in countries where the disease is found Thorough cooking of beef pork and fish

CHAPTER IV

CONDITIONS DUE TO PHYSICAL AND CHEMICAL AGENTS

Electrical Injuries

These are everyday industrial hazards and occur also in regions where heavy lightning discharges are common. Local injury results from contact with a live conductor or live apparatus and varies from a superficial burn to extensive charring of the tissues according to the tension of the current. The general effects are due to electrolytic and disruptive forces and to heat generated by passage of the current. Death may occur instantaneously if not shock is usually profound and the victim may remain in coma for hours. Painful muscular spasms and delirium often follow. The nervous system is most sensitive to electrical interference and cardiac upset in the form of ventricular fibrillation may be induced. Permanent residua such as paraplegia, cranial nerve disturbance and mental defect are found. Psychoneurosis may be the only sequel.

In treatment the first essential is to remove the victim from contact with the conductor if the current cannot be quickly interrupted. To avoid electrifying the rescuer a non-conductor such as a walking stick or wooden pole may be used or the hands protected by dry materials such as thick gloves or a thick woollen or leather garment. If breathing has ceased artificial respiration should be maintained for several hours if need be. Eve's rocking method is convenient until the victim reaches hospital when oxygen by positive pressure and assisted respiration will be substituted. Lumbar puncture may be done to relieve coma and stimulants such as nikethamide given for respiratory or cardiac weakness. Ventricular fibrillation is treated by one or more injections of acetylcholine 1 mg into the left ventricle. Burns are frequently severe and call for expert care.

Effects of Heat

The human body loses heat by conduction convection radiation and evaporation. When the temperature of the air rises above that of the body the first three processes stop or are even reversed. If air movement is slight a blanket of moisture surrounds the body and hampers evaporation and this factor becomes more serious as humidity of the air increases. Two dangerous atmospheric conditions may therefore arise (1) a dry wind of speed 40 m.p.h. or over and temperature of 122° F. Here heating by reversed convection exceeds the heat loss by evaporation. (2) a wet bulb temperature of 90° F. or over. Damage from direct sun is no greater than that from an equivalent air temperature but sunburn is an added danger.

Three clinical patterns are described although intermediate types are common.

1 Simple heat exhaustion. Characterised by circulatory asthenia. Symptoms are weakness headache nausea giddiness and fainting. Muscular cramps may be present and urinary chlorides are reduced. Treatment consists of rest in a cool room and administration of 3.6 pints of water containing 3.6 drachms of salt and flavoured with sugar and lime or orange juice. Recovery is rapid but recurrence is frequent and there is often a psychogenic element.

2 Subacute effects of heat. Has an insidious and apyrexial onset and is a most grave form of heat exhaustion. There is rapid derangement of blood chemistry (dehydration reduction in plasma chloride and alkali reserve increase of non protein nitrogen). The first stage is heralded by apathy personality change insomnia anorexia polyuria and dry skin. Oral temperature may be normal but the rectal is usually raised to 102° F. Peripheral shock speedily follows. If untreated hyperpyrexia meningeal irritation convulsions and coma develop. Malaria diarrhoea and vomiting add their quota of aggravation.

For treatment the patient is put at absolute rest in a cool shaded room having a free circulation of dry air. Fluids and salt should be pushed until a satisfactory urinary and chloride output are obtained. An average daily requirement is 5.6 pints of water and 1 1½ oz. salt which may be taken partly

in capsule form. A fluid balance chart gives useful indication of the amounts of fluid and salt required. If shock is a feature 500 ml plasma should be transfused at the outset. If the patient is unconscious glucose and twice normal saline are given by intravenous drip until diuresis and a positive chloride balance result. 4th to 4rd normal saline is then substituted. Eight to twelve pints may be required to restore fluid balance (See p. 204).

In the hyperpyrexial stage the temperature must be reduced to 102° F as quickly as possible by covering the patient with a wet sheet and allowing an electric fan to play on it. A fall in rectal temperature of 4-6° F indicates that treatment has been successful but vigilance should not be relaxed for at least two hours in case of relapse. Fluid and salt are given according to indications and lumbar puncture is necessary for convulsions or prolonged coma. Circulatory failure is met by oxygen inhalations and stimulants such as intravenous /noradrenaline. Respiratory failure demands artificial or mechanically assisted respiration.

Intravenous quinine should be given on reasonable suspicion of malaria.

3 Acute heat effects. Caused by sudden failure of the heat regulating mechanism. Prodromal symptoms are similar to those of subacute effects of heat but coma, hyperpyrexia and circulatory weakness may suddenly present. Treatment as in subacute heat effects.

Heat cramps may occur alone or in association with the other manifestations of heat effects. Found among the stokehold personnel of steamships and in mine workers they are due to heavy muscular exertion in a hot atmosphere and respond to routine administration of salt and fluids.

Prophylaxis of heat effects. Gradual acclimatisation suitable clothing, cool living-quarters and arrangement of the working-day to avoid strenuous exertion during warmest periods but sleep hours should not be encroached upon.

Routine administration of salt and fluids, restriction of alcohol, suitable and appetising diet, recreational amenities. Detection and treatment of tropical infections, avoidance of anaesthetics, atropine, antipyretics and elective surgery.

during hot periods (unless air-conditioned wards are available) Alcoholics poor sweaters and prickly heat sufferers are candidates for heat effects and should be sent to a cooler climate Persons who have suffered from severe heat effects should move to a more reasonable climate as the risk of further attack is considerable

Sunburn

Severe sunburn occurs in light skinned races and is caused by *injudicious exposure to the ultra violet moiety of direct sunlight* gradual insolation produces a healthy tan Dermal injury of this kind predisposes to other heat effects Suntan oils are liable to cause a frying effect and may interfere with sweating Vanishing cream bases containing chemicals which act as a protective screen e.g. quinine hydrochloride tannic acid glycerol para aminobenzoate may induce skin sensitivity or cross sensitivity but are otherwise unobjectionable

Erythema is relieved by soothing lotions such as calamine liniment but vesicular lesions require full surgical toilet and application of protective dressings such as soft paraffin gauze Hydrocortisone ointment or lotion is an excellent remedy for sunburn

Prickly Heat

For prevention loose fitting open weave garments should be worn and changed frequently Clothing should be conscientiously laundered and not merely dhoibied Adequate fluid and salt intake is desirable Careful drying of the skin after bathing and powdering of the axillæ and groins are important O'Brien regards the over use of soap and bathing as contributory causes He recommended painting the affected areas with 10 per cent alcoholic solution of salicylic acid for a few days to produce exfoliation with subsequent use of lanolin to prevent degreasing of the skin A few days rest in a cool room and application of a salicylic acid sulphur dusting powder are worthy of trial (salicylic acid gr 8 sublimed sulphur gr 6 boric acid gr 4 zinc oxide gr 20 purified talc to 1 oz.)

1 1 000 perchloride of mercury is a useful alternative if applied after bathing and allowed to dry on

Effects of Cold

General effects of cold arise most frequently in those who are inebriated, injured or have lost their way. Poor physical condition, hunger and lack of sleep are important contributing factors. Drowsiness and an irresistible desire for sleep appear together with an euphoric incoherent mood. Cardiac failure results from extensive freezing of the tissues.

The victim should be moved to cover as quickly as possible and the atmosphere gradually warmed. Dry warm blankets, hot water bottles and gentle massage (without allowing the body to cool) are useful and warm sweetened drinks may be given. Stimulants such as nikethamide, adrenaline and later alcohol may be administered if required. Artificial respiration and 1:1000 adrenaline by intravenous drip should be tried in cases showing signs of respiratory or circulatory failure.

Local effects of cold are found in the hands, feet and exposed parts of the body. The nose, ears and cheeks, having little subcutaneous fat, are vulnerable. Freezing may occur within a few minutes of exposure, particularly in a high wind. Prolonged immobility and light garments encourage sluggishness of the peripheral circulation.

Frost bite of the nose and ears may be unrecognized at first by the victim. The stage of stiffness, numbness and waxy pallor is followed by a reactive one. In immersion foot the skin of the affected parts may be waxy pale but is more often dusky and cyanotic. In the stage of reaction pain, hyperaemia, neurovascular change and oedema are common. All stages of skin lesions from superficial ulceration to gangrene may follow.

The patient should be moved to a room having a temperature of 60-65°F. The body is wrapped in warm dry blankets while the affected parts are uncovered, elevated and kept dry. Extensive local oedema calls for skin incision and the affected areas must be cared for with strict asepsis. Antitetanic protection should be given and sepsis and pneumonia treated by antibiotics. Deep ulceration and gangrene require appropriate surgical measures.

Some degree of residual neurovascular impairment is inevitable (coldness, cyanosis, increased perspiration).

Physiotherapy will help in mild cases but sympathectomy may eventually be necessary to improve function and lessen discomfort

Prophylactic principles include suitable diet and avoidance of over fatigue suitable protective clothing changes of dry underwear and socksunction of the extremities and face with water free grease before exposure to cold

Chilblain (Pernio) Areas of localised congestion swelling and itching on the fingers toes and legs which tend to winter recurrence in individuals with poor peripheral circulation The overlying skin may crack, causing superficial ulceration Treatment consists of warm loose clothing of the affected parts fresh air exercise contrast baths and general ultra violet radiation Vasodilators like Ronicol (Roche) and Pernovit (B D H) are of value for severe cases sympathectomy should be considered Locally in the early stages stimulation by diluted tincture of iodine or Balsam of Peru Compound Ointment B N F is helpful for broken surfaces Ichthammol Ointment B P C encourages healing

Effects of Radioactivity

Health hazards incidental to the processing of radioactive materials are considerable Pitchblende the basic ore of uranium and its disintegration product radium are dangerous to miners and smelters because radon is liberated by neutron capture atmospheric elements and contaminants are converted into radioactive isotopes of which some have a long half life (C H) while others have a short half life (N O) The route of contamination is the respiratory tract and lung cancer develops in a high proportion of workers usually after a latent period of fifteen to seventeen years The incidence of this disease has been substantially lessened by dust reduction measures particularly exhaust ventilation Refining processes carry their individual risks for example exposure to uranium fumes may induce a chemical nephrosis Preventive measures include reduction of dust and elaborate personal hygiene A complete outfit of clothing is kept for workshop use only before leaving the workers bathe and change into uncontaminated clothing Eating drinking and smoking are prohibited in the workshop to prevent

ingestion-contamination. Dust sampling and regular medical examination (including estimation of urinary radioactive output) indicate the adequacy of control measures.

Instrument dial painters formerly pointed their sable brushes with the lips, thus ingesting traces of radium paint. Deposition of radium phosphate in the bony compact layer occurred while the spongiosa absorbed relatively little. Osteosarcoma, particularly of the mandible, was common until a less dangerous method of applying the paint was evolved.

The radiation syndrome which complicates extensive radiotherapy and the depression of bone marrow activity which is beneficial in leukaemia and erythraemia are well recognised. A new risk in the shape of heightened incidence of leukaemia has arisen amongst physicians practising radioscopy and among patients extensively irradiated for ankylosing spondylitis.

The operation of an atomic pile is fraught with health hazards on account of the concentration of radioactive materials and the powerful discharge of gamma rays and neutrons. The fission chamber is screened by dense metal and concrete and efficient monitoring systems are employed. Great care is taken in regard to disposal of wastes. The coolant if air is discharged through a sufficiently tall stack to reduce site contamination to a fraction of the safe level. Cooling water and chemical wastes must be trapped and stored until natural decay of radioactivity renders them safe for disposal into streams, etc. Disposal of partly exhausted fissionable materials is by dumping in an isolated site until disintegrated to safe levels or at sea. Manipulation of radioactive substances is rendered harmless by screens and instruments of the lazy tongs type. Exhaust ventilation (with trapping of the exhaust) and periodical medical examination of personnel are essential.

Knowledge of the effects of massive exposure to radioactivity rests upon data from the military bombing of Japan, experimental bombing and accidental contamination. The effects of tactical bombing vary according to whether the explosion occurs high in the air, at ground level or under water. The first produces widespread material destruction

from blast. It is accompanied by a momentary brilliant light and radiant heat flash which can distort metal blister tiles and set woodwork alight far beyond the periphery of the explosion area. A rapidly rising fire ball is replaced by a mushroom shaped vapour cloud which releases a shower of fission product with radioactivity of variable duration (up to one minute). There is a drift down wind and isotopes are formed by neutron capture of Na, Cl and other ions. Strontium 90 is a particularly dangerous fall-out hazard as it gives rise to osteogenic carcinoma. Gamma rays unlike neutrons are widely disseminated.

In ground burst the fission products tend to be driven into the earth and widespread radioactive contamination may persist for several years. In underwater explosion the heat and light flash show much reduced intensity but underwater blast waves and radioactive contamination are serious hazards.

Of the effects of atomic explosion (prior to the advent of the clean hydrogen bomb) blast and flash burning are similar to but much more intense than those produced by high explosive. These are estimated to be responsible for 35 and 50 per cent respectively of casualties from outside the Ground Zero zone. Radiation is an appalling danger on account of the ionising radiation which lasts for a minute or so and the release of gamma rays and neutrons. Within a central area of $\frac{1}{2}$ 1 mile radius death is instantaneous and due indifferently to trauma from flying debris, blast, burning or ionising radiation. Within an outer sector of 1-2 miles radius injury depends on the amount of protection and is caused by gamma rays rather than neutrons. In the peripheral sector of 2-4 miles radius flash burns and variable but sublethal radiation effects are often found again depending on the amount of individual protection.

In the acute radiation syndrome of the central zone the bulk of the damage is due to neutrons which are absorbed into the skin and subcutaneous tissues. Initially shock, vomiting and prostration are marked. If the victim survives there is a quiet interval after which pyrexia, vomiting, diarrhoea or intestinal obstruction from paralytic ileus supervene. Severe local injury such as oedema, ecchymoses

and skin vesication or sloughing occur. In milder cases from the middle zone shock and other manifestations may be delayed for two to six weeks or may be absent. Later wide spread tissue destruction becomes apparent and the order of decreasing vulnerability is lymphatic tissue, germinal epithelium, bone marrow, intestinal mucosa, skin. There is a rapid fall in all blood cells with angiose inflammation of the oropharynx and hæmorrhagic septicæmia as in pan-hæmocytopenic states generally. Temporary sterility and a high abortion rate follow mass radiation and cataract has been reported. Impairment of growth of male children has been noted also increased neoplastic tendency (leukæmia, skin tumours). Chromosome fracture and gene mutation may be induced with results which cannot be advantageous to the community.

Treatment of atomic radiation casualties must be a problem of distressing magnitude. Protection is by deep shelters or by the familiar surface shelters of the last war reinforced by substantial layers of concrete or rammed earth. Personal protection would be by covering the body as completely as possible with light coloured material. Aluminium foil clothing has been suggested for rescue workers and monitoring would be necessary to decide safe working spells. Decontamination units would be similar to those arranged for poison gas but radioactivity cannot be diminished by chemical treatment and only washing is useful. Food stores and water supplies would need careful scrutiny. Tinned foods are reasonably protected, wrapped solids would be safe if the outer layer were removed but foods of porous consistency like bread are unusable. Deep well water is usually safe.

In view of the large number of casualties likely to occur therapeutic resources inadequate at best must be concentrated on those who have a chance of recovery. Prominence of fever, intestinal irritation and epilation are of grave portent. Treatment of the acute stage is primarily that of shock, pan-hæmocytopænia, enteritis, burns and sepsis. It includes complete rest, warmth, blood and plasma replacement together with fluids and electrolytes as required, antibiotics, cortisone and appropriate surgical treatment. (See G. D. Kersley *Brit med J* 1958 II ■ 379.)

Alcoholism

Acute alcoholism An emetic should be given (sodium chloride or bicarbonate 1 oz. to 1 pint of warm water). The sufferer is then encouraged to take plenty of bland fluid. If comatose the stomach should be washed out using 3 or 4 pints of warm sodium bicarbonate solution (2 drachms to the pint) and 10 oz. of strong black coffee may be left in. He should be put to bed kept warm and a free airway maintained. Always examine for injury (especially cerebral) and disease. Stimulants such as caffeine sodium benzoate or nikethamide should be available and artificial respiration may be necessary. Cyanosis is met by oxygen inhalation. An intravenous injection of vitamin B₆ (pyridoxine) 50-100 mg. is reputed to exert a prompt sobering effect. An early morning saline, a breakfast of toast, coffee and fruit juice followed by a dose of soluble aspirin will do much to restore well being. Chlorpromazine (Largactil M & B) 25 mg. three or four times daily is a useful calmative.

Chronic alcoholism The aims of treatment are to provide mental and physical rest to ensure adequate nourishment and to rebuild some measure of psychological stability.

Residence for several months in a home or institution is desirable as the ministrations of misguided relatives are likely to conflict with the practitioner's therapeutic intentions. Willingness to undergo the prolonged course of treatment requisite for thorough cure is a hopeful prognostic portent.

One to two ounces of saturated magnesium sulphate solution is a useful preliminary. A high caloric dietary should be ordered and liberal fluid intake encouraged. Moral suasion is usually necessary at first as nourishment is ordinarily an insignificant item in the alcoholic's routine. Some degree of hypovitaminosis follows the habitual neglect of food and the leaching out effect of alcoholic beverages. Vitamin B concentrates should be given by vein at first (Parentrovite Vitamins Ltd. one high potency ampoule daily) and later by mouth.

Immediate and complete withdrawal of alcohol is the best tactic and is free from the risks associated with it in the lay mind. *Tapering off methods predicate a degree of will power which seldom exists.* Exceptions may be made in the

case of elderly and enfeebled addicts and those who must be treated in their homes. In such cases the allowance of alcohol is reduced by 25 per cent daily and the withdrawal period made bearable by the administration of atropine and atychinin in combination with tonics and sedatives.

Amphetamine is sometimes of assistance in combating the severe depression incidental to reduction of alcoholic intake. One tablet of dextroamphetamine sulphate (5 mg) may be taken with breakfast and morning coffee.

The conditioned aversion treatment is useful in young and robust alcoholics in that it provides a breathing space of sobriety during which effective psychotherapy may be employed. The patient is given a helping of his favourite beverage (spirits should be diluted with an equal amount of water) also an intramuscular injection of apomorphine gr $\frac{1}{4}$ repeated if necessary in fifteen minutes. Ten per cent of patients do not vomit but this does not prejudice the cure. Vomiting is followed by a period of sleep lasting about two hours. Further doses of alcohol are offered at three or four hourly intervals and if swallowed are followed by an injection of the vomiting dose of apomorphine. No food or drinks (except alcohol) are allowed at this stage of treatment. Washing and mouth toilet are forbidden.

After two or three days alcohol becomes increasingly repulsive and despite severe thirst the patient will refrain from taking it. Without the establishment of intense thirst it is impossible to measure his aversion to the proffered drink. Towards the end of treatment the patient sweats profusely, persistent vomiting occurs and the blood pressure falls (treatment is stopped when levels below 100 mm are reached). He is then allowed to take bland fluids, eat light diet and to wash. The apomorphine injections are continued in dosage of gr $\frac{1}{4}$ six hourly for twenty four hours followed by gr $\frac{1}{4}$ six hourly on the final day. Daily injections of intravenous or intramuscular Parent ovite should be given.

Tetraethylthiuramdisulphide (disulphuram, Antabuse) raises the blood acetaldehyde level without affecting the metabolism of alcohol. The Antabuse-alcohol reaction is due to interference with acetaldehyde oxidation and this substance exerts a depressant action on the myocardium,

manifested clinically by hypotension and bradycardia. The initial phase of treatment should be conducted in hospital. One 0.5 G tablet of Antabuse is given and followed in one hour by 15-20 ml of the favoured spirit. The reaction consists of flushing of the face and neck, sense of constriction in the chest, faintness and general unease. The reaction induced by small doses of alcohol is unpleasant but not dangerous. The same procedure is gone through each day with gradual increase in alcohol dose until maximal safe reaction is reached as judged by blood pressure readings. The patient is then discharged with instructions to reduce the Antabuse dose to one half tablet daily after a week and to one-quarter tablet after two weeks. His conditioning by this background of Antabuse continued over weeks or months is revived if he essays a drink; this experience with psychiatric guidance may lead to cure.

Contra-indications to Antabuse treatment are diabetes, hepatic cirrhosis, nephritis, epilepsy and pregnancy. It is essential that the patient be free from cardiovascular disease and that he have a strong will to be cured. An alcoholic break-out may be fatal and the method should not be used with weak-willed and compulsive drinkers. Psychiatrically unstable subjects are also unsuitable as they may develop manic reactions as a side effect of acetaldehyde hold-up. This treatment is therefore expedient in only a small minority of alcoholics. Intravenous ascorbic acid, ephedrine sulphate and oxygen inhalations have been used to cut short severe reactions. Paraldehyde should not be given in association with disulphiram.

Hydrotherapy has a valuable calming effect on sleepless and restless patients in the stage of convalescence. Physiotherapeutic resources such as massage, exercises and diversional therapy are used to expedite physical rehabilitation.

Sufficient sedative must be given to ensure sound sleep. Casual or routine sedation, especially with barbiturates, should not be countenanced on account of the addiction risk. Frequent change of hypnotic is desirable and the identity of the drugs used should not be disclosed to the patient. The following do not tax the already damaged liver and are therefore suitable.

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Paraldehyde 2-4 drachms twice or thrice daily Where gradual withdrawal is being used this drug if added to the spirit allowance will by virtue of its unpleasant character help to establish a negative conditioned reflex

Phenobarbitone gr 1 thrice daily

Soluble barbitone gr 10-15 in the evening will produce sound sleep

Bromide and chloral mixture (gr 15 of each) should be substituted when immediate objectives have been gained

Some derive confidence from tranquillisers e.g. promazine hydrochloride Sparine Wyeth meprobamate Equanil Wyeth The former is given in oral dosage of 50-150 mg four hourly during the withdrawal stage and later in one half this dosage for relief of depression irritability and nausea

A complete physical and psychiatric evaluation of the patient is necessary Septic foci and painful conditions must be dealt with His mode of life should be reviewed and the importance of ample relaxation and fresh air exercise emphasised Mental conflict arising out of unharmonious domestic social or business environment should be discussed and the possibilities of solution or rationalisation canvassed The futility of alcohol as an escape should be indoctrinated

Alcoholics Anonymous A body of ex-addicts who have obtained insight into the malady and realise that no alcoholic is ever cured but that a determination not to take the first drink is a sound practical philosophy By banding themselves together their experience and help are freely available to less fortunate brethren They in turn must derive considerable moral reinforcement from their praiseworthy rôle of bell-wethers of the flock.

Delirium tremens This is a toxic psychosis requiring prompt isolation and treatment without the former supervision is impossible The existence of an acute infection such as pneumonia should not be overlooked Complete rest in bed is essential and the services of experienced and sympathetic attendants are invaluable Restraint is harmful, and unnecessary if effective sedation is arranged for An aperient should be administered and a semi-solid diet of high caloric value pushed Alcohol is withdrawn morphine avoided but sedation maintained by paraldehyde phenobarbitone or

bromide and chloral mixture Circulatory weakness calls for stimulants such as caffeine or pholedrine

Sedation must be maintained for several days to permit resolution of the psychosis and after treatment is that of chronic alcoholism Liberal vitamin B and glucose dosage by vein ■ most important Some alcoholics respond well to calmatives like chlorpromazine and meprobamate

Dipsomania. A form of recurrent compulsive psychosis which ■ resistant to treatment Psychotherapy may be tried during the quiescent phases

Morphine Poisoning

Acute Emetics are unreliable so give activated charcoal or universal antidote six teaspoonfuls in water then wash out the stomach with potassium permanganate 1 1000 A good airway must be maintained by endotracheal tube if necessary also oxygen and mechanically assisted respiration if required Shock ■ combated by intravenous saline and noradrenaline milder degrees respond to methylamphetamine hydrochloride 10-15 mg by vein Nalorphine (Lethidrone ■ W) counteracts the respiratory depression so fatal in morphine poisoning Dose 5 mg intravenously if respiration does not deepen within a few minutes give 10 mg followed by 15 mg at twenty minute intervals until the patient is awake and breathing normally

Morphine addiction The general management ■ similar to that detailed for alcoholism and it is important to relieve conditions causing pain or discomfort

Sudden withdrawal of morphine entails intense mental suffering and perhaps collapse The consumption of the drug should be reduced by 25 per cent daily and during the tapering off period some other hypnotic is given liberally The most serviceable substitutes are phenobarbitone gr 1 thrice daily paraldehyde 3-4 drachms twice daily sodium pentobarbitone gr 1½-3 thrice daily These drugs are also capable of arousing addiction and in course of a few days they should be relegated in favour of a milder hypnotic such as carbromal or bromide and chloral mixture Reserpine (Serpasil Ciba) aids withdrawal 2 mg doses being given initially

Rectal and colonic instability is a troublesome and exhausting complication of withdrawal treatment and the best corrective is a daily saline enema and small doses of tincture of belladonna by mouth

Barbiturate Poisoning

May occur accidentally during anaesthesia and being in wide circulation these drugs are popular with would be suicides. The gaily-coloured proprietary capsules while useful for identification purposes are unfortunately attractive to children.

Gastric lavage is good first aid treatment within three hours of swallowing the poison. The prognosis and method of treatment depend to some extent on whether the barbiturate belongs to the short action or prolonged action group. With the former (pentobarbitone cyclobarbitone isomethyl barbituric acid) unless dosage is large or liver disease present the risk to life is from respiratory depression. In the latter case (phenobarbitone allobarbitone barbitone) the cause of death is usually aspiration pneumonia particularly if renal impairment is present.

Mild case of intoxication with short action drugs may be conscious or rousable on admission to hospital for these gastric lavage with two pints of tap water or normal saline is done and the patient allowed to sleep it off. After heavy dosage with short action or overdosage with prolonged action drugs the patient will show signs of severe intoxication i.e. incoherence rousable only with painful stimuli coma. Treatment consists of warmth (not over heating) maintenance of a clear airway by endotracheal tube aspiration of pharyngeal secretions and elevation of the foot of the bed. Oxygen should be given by H.L.B. mask (8 litres per minute) also penicillin (500 000 units six hourly) to ward off pulmonary infection. If haemoconcentration and circulatory collapse are imminent 2-3 litres of 5 per cent glucose saline is given by intravenous drip with noradrenaline added as required. Constant observation and expert nursing are essential (frequent change of posture care of mouth and pressure points catheterisation).

The place of analeptic drugs in barbiturate poisoning is

much disputed. Overdosage is difficult to avoid and often dangerous. Many prefer the conservative routine outlined above with the addition of vitamins to the intravenous fluid as in Gould's treatment (see below). Leptazol, nikethamide and picrotoxin have passed out of general use. amphetamine sulphate ■ relatively safe (10-25 mg intravenously initially and repeated hourly). Caffeine sodium benzoate is harmless and may be given intravenously (0.5 G half hourly for three doses). Bemegride (Megumide, Nicholas) ■ the least obnoxious and most reliable analeptic and 10 ml of the solution may be injected into the delivery tube of the drip set every three to five minutes until a safe state is reached (response to stimuli, pupillary, corneal and pharyngeal reflexes present) from which the patient will wake in up to 8 hours although he may relapse and require further dosage. Average total requirement of bemegride is 200 ml. Toxic signs (retching, twitching of the finger muscles) call for interruption of therapy.

Gould's routine for delirium, psychosis and coma due to narcotics (including alcoholism and delirium tremens) ■ intravenous infusion of the following: aneurine hydrochloride 1 G, nicotinamide 200 mg, pyridoxine 200 mg, ascorbic acid 1.5 G, 10 per cent glucose solution 100 ml and distilled water or normal saline to 250-300 ml. The initial infusion should occupy forty-five to seventy minutes and may be repeated once if necessary, then two further injections of half the above amounts are given at intervals of four to eight hours according to progress.

Lead Poisoning

Acute. Wash out the stomach thoroughly with 1 per cent sodium sulphate solution, leaving 2 oz in the stomach. Demulcents are useful, also calcium gluconate. 5-10 ml of 10 per cent solution by vein for colic. Morphine may be necessary.

Chronic. The patient should be removed from contact with the metal. Colic and cramps are rapidly relieved by intravenous injection of 10 ml of 10 per cent calcium gluconate solution and the administration of aperients. Chelating agents are effective in plumbism. Soluble non-ionic chelates

are formed only with polyvalent metallic ions. They exchange these for less toxic ions in the organic complex thus causing their functional removal from the body fluids. With calcium disodium versenate (E.D.T.A.) lead displaces the calcium component. This lead chelate is water-soluble non ionisable and non toxic. Dose 0.5 G per 30 lb body weight hourly added to an intravenous drip with a daily maximum of 1 G/30 lb and a weekly limit of 5 G/30 lb. Ten-day courses with weekly intervals are usual. Overdosage with sodium calciumedetate may cause reversible nephrosis. Disappointing in organic lead compound intoxication its use has been suggested in haemochromatosis. Janner Wilson's disease and as an *in vitro* anticoagulant. It has been used to sequester plutonium accidentally absorbed also corneal calcium deposits and as a local application to chrome ulcers.

Prophylaxis

Routine physical examination (including blood-count) of lead workers on entrance and at regular intervals. The use of protective garments and respirators. Washing of hands before eating. meals should be taken in a canteen and not in workshops. Wet grinding of lead pigments. Efficient local exhaust ventilation of workshops. Dilute sulphuric acid $\frac{1}{2}$ 1 drachm daily in lemonade. Avoidance of lead piping for plumbo-solvent water supplies and for beer pumps.

Arsenical Poisoning

Copious gastric lavage using 2 per cent. sodium bicarbonate in 1 per cent. sodium thiosulphate followed by demulcents such as egg white. B.A.L. is of considerable value in arsenical poisoning (2-4 ml of 5 per cent oily solution intramuscularly four hourly for the first day twice on second and third days and daily thereafter for ten days).

Carbon Monoxide Poisoning

The patient must be moved out of the contaminated atmosphere immediately and the receiving room should have a free circulation of fresh air. Continuous oxygen inhalation by tent or B.L.B. mask should be arranged and

artificial respiration by Eves method or mechanical respirator given if required. The patient must be kept warm and with a clear airway and stimulants e.g. nikethamide injected if sign. of circulatory failure appear. Blood transfusion and intravenous procaine have also been found of value.

In view of the firm nature of the carboxyhaemoglobin affinity complete rest and oxygen inhalation are often necessary for many hours after apparent recovery and supervision should continue for several weeks. Progress may be gauged by spectroscopic examination of the blood.

CHAPTER V

VITAMIN DEFICIENCIES

Vitamin A

Xerophthol or vitamin A proper is one of a group of substances having similar action and the principal provitamin is carotene. The vitamin has been synthesised by Isler and others. The main function of this group is to promote the integrity of epithelial structures. Lack causes deficiency of dark adaptation owing to defective synthesis of visual purple and visual violet and night blindness follows. Even after prolonged deprivation defective dark adaptation occurs in a few subjects only and no other condition attributable to the deficiency has been discovered. Other manifestations of experimental deficiency in animals are xerosis of the cornea and conjunctiva, papular skin rashes and keratinisation of various epithelial surfaces which facilitates infection. Thus squamous metaplasia of pulmonary epithelium leads to inflammatory change and in the case of the renal pelvis encourages formation of calculi. This vitamin is necessary for growth of bone; overdosage leads to abnormal periosteal bone deposition.

Deficiency occurs in starvation states and in fat free diets; defective absorption is found in sprue and coeliac disease. The carotene vitamin A conversion takes place in the bowel and the vitamin is stored in the liver; disease of the latter organ will induce devitaminosis.

Rich sources of vitamin A are fish liver oils and the flesh of oily fish. Butter is a relatively good source (60 i.u. per G.) and human milk during the early part of lactation. Carotene occurs in green vegetables (9 i.u. per G.) and carrots (19 i.u. per G.). Mixtures of vitamin and provitamin are found in tomatoes, peaches and apricots.

The average daily requirement for a child is 4 000 i.u. and 3 000 i.u. for an adult, but this figure must be doubled during

BPC for curative treatment double this dose is sufficient
Overdosage may cause kernicterus

Vitamin K is a useful addition to the pre and post operative management of jaundiced and hepatic subjects
Injections of 5-10 mg. of menaphthone are ordered several times daily for three days before and following operation afterwards continuing with oral dosage Menaphthone has been used prophylactically in sprue and colitis syndromes
Phytomenadione vitamin K₁ (Konakion Roche) controls bleeding caused by coumarin and phenindione overdosage
Dose 10 mg. intramuscularly or 1-2-10 mg. capsules orally
These drugs have no value in haemorrhagic states other than those resulting from hypoprothrombinemia They have been reported useful in some cases of urticaria and chilblains and during salicylate therapy

Vitamin B

Members of the B complex are found in many foodstuffs
At least thirteen factors have been identified but their significance in the human economy has not yet been defined

Vitamin B₁ (anewine hydrochloride thiamine) Antineuritic or beri beri factor Occurs in yeast wheat germ liver kidneys lean pork peas and beans It appears to function as a co-enzyme in the pyruvate stage of carbohydrate metabolism and increased blood pyruvate affords a convenient test for deuteraminosis Vitamin B₁ is essential for nutrition of nerve cells probably by promoting glycolysis within the nervous tissues The features of B₁ deficiency are anorexia vomiting (which aggravates the deficiency) constipation weight loss increased fatigability dyspnoea oedema tachycardia and cardiac enlargement loss of Achilles reflexes and vibration sense wrist and foot drop and tenderness of the calf muscles

Beri beri is associated with deficiency of this vitamin but other considerations such as the proportion of carbohydrate in the dietary are of importance This disease does not develop under conditions of complete starvation but appears if excessive carbohydrate is given without adequate vitamin B₁ particularly in circumstances of strenuous physical exertion

Beri beri is endemic in Eastern countries amongst populations whose staple diet is cereal. Bleaching or milling denudes the cereal of bran and endosperm which contain the vitamin and all whole extract of rice polishings has long been recognised as curative. High-extraction flour although unpalatable to many and unpopular with bakers conserves this vitamin to the community which otherwise is diverted to animal feeding. The full blown syndrome of polyneuritis (dry beri beri) myocardial weakness and oedema (wet beri beri) gastro-intestinal or mental upset (Wernicke's encephalopathy) is rarely encountered in this country but polyneuritis and acute cardiac failure may be found in elderly persons suffering from chronic undernutrition in diabetics and alcoholics (particularly those engaged in heavy manual occupations). Conditioned deficiency may occur also in colitis sprue and intestinal obstruction where absorption of the vitamin is defective. Synthesis in the bowel is inhibited by bacteriostatic drugs.

The normal daily adult requirement is about 1.2 mg. (330-660 i.u.) Larger amounts are necessary in childhood pregnancy lactation diabetes hyperthyroidism and in strenuous physical exertion.

Sources (i.u. per g.)

Wheat germ	9.5	Yeast	4.6-8
Bacon	4	Oats	1.8
Egg yolk	0.5	Wholemeal	0.9-1.7

Aneurine Hydrochloride Tablets B.P. 3.25 mg.

Injection of Aneurine Hydrochloride B.P. 25 mg. per ml.

Curative dose 20-100 mg. daily

Acute beri beri requires rest in bed a light diet containing liberal amounts of first-class protein (milk, cheese, eggs, soups, etc.) and venesection if the right heart is labouring. Intravenous dosage of aneurine (50-100 mg. daily) should be given until improvement is manifest. Oral dosage may then be substituted. For treatment of polyneuritis and myocardial failure see appropriate sections.

Vitamin B₂ includes several factors

Pellagra prevention factor nicotinic acid. Has been

synthesised and forms part of a co-enzyme oxidative system essential for cellular metabolism. The characteristic features of pellagra are glossitis stomatitis symmetrical dermatitis with increased pigmentation of the exposed skin enteritis and mental disturbances. Mild cases showing skin and mouth lesions are not infrequent in this country but the disease is endemic in areas where maize is the staple diet. The normal requirement of nicotinic acid is about 10 mg daily. It circulates in the body as nicotinic acid amide and it is usually administered in this form on account of unpleasant flushing and tingling of the face which the acid causes. The richest natural sources are yeast wheat germ liver fish and pulses.

Pellagrins should have a liberal diet containing 100-150 G protein and alcohol is forbidden. The curative dose of nicotinamide is 250-500 mg daily orally or 80 mg by vein. Moderate degrees of anaemia will respond to iron but blood transfusion is necessary in severe cases. Suitable protection from sunlight must be devised and soothing lotions prescribed for the dermatitis.

Riboflavin A co-enzyme for the activation of certain respiratory ferments such as cytochrome. It is obtained synthetically and in milk meat liver eggs fish green vegetables and fruits. The normal requirement is about 2-3 mg daily. Deficiency causes cheilosis angular stomatitis desquamative glossitis kerato-conjunctivitis and seborrhoeic dermatitis of the pinna and nose. For treatment 10-20 mg daily by mouth is sufficient in most instances but temporary resort may be necessary to the intravenous route (5 mg thrice daily).

Vitamin B₃ (pantothenic acid) Found in all animal tissues (notably liver and kidney) in yeast wheat and cultures of fungi and bacteria. The acid has been synthesised. It is essential to many species and is an activator of the acetylation enzyme systems. Experimentally it prevents achromotrichia but this has no validity for the human species. The substance has been used in treatment of deprivation states particularly the Indian burning feet syndrome.

Vitamin B₆ (pyridoxine) Present in meat liver yeast egg yolk, peas and soja beans and has been synthesised. In animals deprivation causes dermatitis hypochromic anaemia

and neuronic degeneration. In man seborrheic dermatitis and hypochromic anemia follow deficiency of this factor. Pyridoxine has been used in drug reactions (100-200 mg daily by mouth or vein in radiation sickness and hyperemesis gravidarum (20-100 mg daily).

Folic acid (pteroylglutamic acid) Present in green leaves and all animal tissues and produced synthetically. Is a growth factor for *Lactobacillus casei*. Other similar substances have been identified e.g. folinic acid (citrovorum factor) to which folic acid is probably converted in the body by indirect action of ascorbic acid.

The substances of this group show a haemopoietic action but their relationship to vitamin B₁₂ is still obscure. They are used for correction of macrocytic anemias associated with sprue, steatorrhea, pregnancy and nutritional deficiency.

Vitamin B₁₂ (cyanocobalamin) Rickes and Lester Smith isolated a cobalt-containing pigment from liver extracts which is probably identical with the extrinsic factor of Castle. It is produced commercially as a by product of streptomycin manufacture by deep fermentation of *Streptomyces griseus*. An active haemopoietic in Addisonian and other macrocytic anemias.

Choline A constituent of the B complex which functions biochemically as a transmethylation agent. Experimental evidence suggests that it protects the liver from fatty degeneration. It has been used (with doubtful effect) for prevention or reversal of post hepatic and cirrhotic liver damage.

Vitamin C

The antiscorbutic vitamin is ascorbic acid (hexuronic acid). The natural substance is found in many fruits and vegetables including black currants, strawberries, citrus fruits, tomatoes, potatoes, swedes, brussels sprouts and cabbage. Its function is enzymic in the oxidation of aromatic amino-acids, and it is concerned with the integrity of colloid matrix structures e.g. collagen. The daily requirement is about 30 mg; this is increased three to five fold during pregnancy, lactation and acute infections. The following contain 30 mg ascorbic acid.

AIDS TO MEDICAL TREATMENT

Fresh orange juice	1½ 5 oz
Ministry of Food orange juice	½ oz
National rose hip syrup	½ oz
Cooked new potatoes	3 6 oz
Fresh tomato purée	4 oz

Vitamin C deficiency manifests itself by increased vascular permeability leading to hæmorrhages into the skin subcutaneous and subperiosteal spaces. The mechanism of capillary fragility does not depend on ascorbic deficiency alone but also on lack of flavones e.g. citrin quercitrin hesperidin. Ascorbic acid is essential for maturation of erythrocytes in the bone marrow and for wound healing. Deficiency causes interference with osseous development the layer of provisional bone remaining wide unorganised and readily frangible. The diaphyseal shaft shows rarefaction with sub-periosteal hæmorrhages.

The clinical signs of scurvy vary according to the extent and duration of the ascorbic deficiency. Early signs in infants and children are loss of appetite fever sore mouth and tender limbs later anaemia becomes marked and hæmorrhages occur into the mouth skin orbit muscle layers under the periosteum or into the epiphyses of long bones. A breast fed infant normally obtains 30 mg of vitamin C daily in the milk but minor degrees of deficiency are common in hand fed infants because cows milk is an unreliable source of this vitamin. When fruit juice is unavailable or ill tolerated a daily dose of 30 mg ascorbic acid should be given from birth. Care must be taken to fortify prescribed diets with this vitamin. Peptic ulcer diets in particular tend to be scorbutic.

Adult scurvy is occasionally found in eccentrics and in elderly and enfeebled subjects living alone. The signs are hyperkeratosis of the hair follicles ecchymoses spongy and bleeding gums with loosening of the teeth. Inertia normochromic anaemia oedema and ulceration of the legs follow and in severe cases bleeding into the knee joints and kidneys occurs. Treatment consists of revision of the diet and administration of 200 mg of ascorbic acid by vein daily for seven days similar dosage is subsequently continued by mouth.

Mouth lesions require citric acid mouth wash (4 drachms of saturated solution to 8 oz water) and dental treatment when the deficiency has been corrected. Liberal iron therapy is beneficial in anemia. Hematomata are treated by immobilizing the limbs with sandbags or light splintage.

CHAPTER VI

DISEASES OF THE DIGESTIVE SYSTEM

DISEASES OF THE MOUTH AND PHARYNX

Acute Stomatitis

The causes of this condition are local such as lack of dental hygiene and general such as acute leukaemia neutropenia scurvy gastric upsets metallic poisons and severe infections e.g. typhoid fever. Treatment must be directed primarily to the cause. Simple stomatitis responds to frequent mouth cleansing particularly after meals with mild antiseptics such as 1 per cent. each of sodium perborate and sodium chloride. Mandil's paint is also effective. Hydrogen peroxide may be used occasionally but is irritant on prolonged application. In enfeebled patients lubrication with glycerin containing a few drops of lemon juice will prevent drying of the mouth and lips.

Thrush occurs most frequently in hand fed infants and is an index of unsatisfactory hygiene.

Ulcerative buccal lesions respond quickly to application of 1 per cent. aqueous gentian violet solution. Hydrocortisone antibiotic applications have been found of value for recurrent aphthous ulcers and labial herpes.

Gangrenous stomatitis is a phagedenic ulceration of the buccal surface with severe constitutional reaction. It is occasionally seen in malignant exanthemata and blood dyscrasias. Tube feeding is usually necessary and vitamin concentrates should be added to the feeds. Peroxide mouth washes are helpful. Penicillin in liberal dosage by injection is often effective but the broad spectrum antibiotics tend to cause denudation of the buccal mucosa. Anaemia must be remedied by blood transfusion if necessary. In neglected cases plastic surgery may be required later for correction of soft tissue defects.

Vincent's Angina Manifests itself as a hypertrophic and hyperæmic condition of the gingival margins. Bleeding and fetor are common. Secondary ulcers with false membrane formation occur on the palatal buccal and tonsillar mucosa. Ulcerated surfaces should be painted with 1 per cent gentian violet, and potassium permanganate mouth washes (1 : 1000) given. Where lesions are extensive injections of procaine penicillin or oral penicillin should be given, and an adequate intake of vitamins B and C assured.

To avoid relapse necessary dental treatment is carried out during a quiescent phase. The patient should be instructed in dental hygiene including the cleansing of inter-cervical dead spaces and the principles of gum massage. The patient's tableware should be marked and kept for his exclusive use.

Pyorrhœa Alveolaris

Careful dental overhaul is the first necessity. Devitalised and crowned teeth should be extracted and all doubtful teeth regarded with distinct prejudice. Partial dentures must as a rule be sacrificed likewise fixed metal bridge work. Scaling and polishing are required at regular intervals to prevent tartar concretions. Chromic acid applications are advantageous in some cases. The patient should be instructed in the proper use of dental points and toothbrush. Digital gum massage is helpful in early cases if properly performed. Non-pulsa-tious foods which require brisk chewing e.g. raw apples provide physiological massage.

More advanced cases show interdental pockets and purulent discharge. Penicillin applications will arrest the pyogenic process temporarily but while the pockets remain re-infection is inevitable. Gingivectomy gives excellent results in suitable cases by abolishing the pockets. Dental clearance is the only remedy in severe and long standing cases.

Pharyngitis

Acute Frequently due to irritation, e.g. tobacco or exposure to cold or damp. When it occurs as part of a common cold or tonsillitis the patient should remain in bed until the infection has subsided. An alkaline mixture should be ordered with gargles of dilute Compound Glycerin of

Thymol B.P.C. or aspirin For relief of irritating cough
Codeine Linctus B.P.C. and spraying with 0.5 per cent
ephedrine sulphate in normal saline are useful

Chronic Irritants such as tobacco and alcohol should be
avoided and dental tonsillar or nasal sinus infection
eradicated Nasal obstruction must be relieved General tonic
measures and local astringents are indicated

DISEASES OF THE OESOPHAGUS

Acute Oesophagitis

May be caused by swallowing irritant or hot fluids
impaction of a foreign body or by over long retention of a
gastric tube Treatment is directed to the cause Feeding can
offer a difficult problem and resort to intravenous infusion
of glucose amino-acids and salt solutions may be imperative
Rupture of the damaged oesophageal wall with infection of
the mediastinum is a grave complication, sometimes remedi-
able by emergency surgery and energetic antibiotic therapy

Oesophageal Stricture

Fibrous stricture may be a sequel to chemical, traumatic or
peptic ulceration or to gummatous infiltration Lesser grades
are relieved by oesophagoscopy and dilation under direct
vision repeated at intervals as necessary Gastrostomy
with retrograde dilation of the stricture may be required for
those involving the lower end of the oesophagus Excision
of the stricture will give relief in suitable cases

In infants congenital stricture may be due either to the
presence of a segment of imperfectly developed oesophagus
or to a short oesophagus with the gastric cardia situated in the
thorax The differentiation is a radiological one Treatment
is by repeated bouginage Congenital oesophageal atresia is
fatal unless promptly recognised and treated by plastic repair

Oesophageal Carcinoma

Careful dietetic supervision is necessary in the later stages
nourishing liquid foods such as milk, soups and custards are
indicated When mouth feeding becomes impossible on

account of obstruction some relief may be given by insertion of a Souttar's tube. Gastrostomy prolongs life and increases comfort and it should not be unduly delayed. Radical surgery of oesophageal neoplasms has become a feasible routine. Radiotherapy has some palliative value in other cases.

Oesophageal Peptic Ulcer and Hiatus Hernia

Caused by ulceration of ectopic gastric mucosa situated just above the cardiac sphincter. It may follow prolonged vomiting, either post-operative from intestinal obstruction or in pregnancy. Hiatus hernia is a constant finding. For treatment the patient should be nursed as far as possible in the sitting up position and a peptic ulcer routine instituted. Solid food is withheld for some weeks until disappearance of the characteristic lower sternal pain. Obesity must be corrected. Gross or long continued bleeding causes anaemia, which should be treated by intramuscular iron. Afterwards the patient must acquire the habit of thorough mastication and each meal should conclude with a dose of antacid and a few mouthful of water to free the oesophagus of gastric acid.

Scarring may give rise to stricture which requires dilatation under direct vision or if severe resection. Large hiatus hernias and those causing persistent symptoms should be treated surgically.

Plummer-Vinson Syndrome

This condition occurs in debilitated females of middle age. Gastric achylia and atrophy of the buccal and pharyngeal mucosa are always present and often a microcytic anaemia. The complaint is of difficulty in moving food masses from the hypopharynx into the oesophagus.

All measures calculated to improve the patient's nutrition should be employed. A liberal semi-solid dietary with reinforcements of eggs, beef tea and casein digests will encourage gain in weight. Anaemia should be combated by intensive iron therapy (See p. 173). Dilatation of the upper portion of the oesophagus by bougies is done by oesophagoscopy and repeated as necessary. The dysphagia may be aggravated by a mucosal web or shelf in the hypopharynx.

which should be divided. Some of these patients develop post-cricoid carcinoma.

Achalasia of the Cardia. Cardiospasm

This condition should be recognised early otherwise extensive dilatation of the œsophagus will take place. Temporary relief of mild cardiospasm follows the inhalation of amyl nitrite or the subcutaneous injection of atropine sulphate gr $\frac{1}{4}$ five to ten minutes before meals.

Negus's hydrostatic dilator is usually effective in early cases. In long standing cases where ulceration of the œsophagus complicates the picture the use of dilators is not without risk here gastrostomy with dilation of the cardia or a cardioplasty operation is to be preferred.

Œsophageal Diverticula. If situated in the upper œsophagus should be excised but those in the thoracic œsophagus only if giving rise to symptoms.

DISEASES OF THE STOMACH

Acute Gastritis

If due to a known irritant this should be removed by repeated washing out of the stomach through a soft stomach tube using in all about two gallons of warm water containing the appropriate antidote. Finally a demulcent such as egg white, starch or gruel may be left in the stomach. Shock and collapse must be treated by elevation of the foot of the bed and stimulants e.g. caffeine sodium benzoate, nikethamide, blood or plasma transfusion, noradrenaline by vein. Jejunostomy may be necessary to save life.

Acute gastritis may result from the ingestion of unwholesome or unsuitable food. Nausea and vomiting are usually prominent. The patient should be kept in bed and the diet reduced to frequent small doses of bland fluids such as barley or albumin water and diluted fruit juice. When the symptoms have abated gradual restitution of diet may be permitted. A gastric sedative such as Aluminium Hydroxide Mixture B.N.F. is useful in the early stages.

Chronic Gastritis and Dyspepsia

Systematic survey of the patient's state and environment is an essential preliminary. Faulty dietetic habits, poor working conditions and excess of tobacco or alcohol must be remedied before success in treatment can be looked for. Physical examination should be made to exclude the presence of morbid conditions such as cardiovascular or renal disease or anæmia. Attention should then be focused on the abdominal viscera as gastric symptoms may be the only manifestation of abnormalities of the bile tract, appendix or intestine. Pyorrhœa, dental inadequacy and morbid nasopharyngeal states have an adverse influence on gastric function. Finally the digestive processes should be investigated by fractional test meal and opaque meal examination and gastroscopy will often yield valuable information. By adoption of a routine for investigation much useless treatment and needless suffering can be avoided.

The patient's mode of life should be recast on sound hygienic lines. A holiday from business worry or from exacting relatives will often terminate a dyspeptic habit. Rest and suitable outdoor recreation are important and regular meal hours are to be observed. Diet should be liberal and easily digested. Meals should be compact, eaten dry and thoroughly masticated. Fluids are best taken between meals.

The patient's dietetic preferences should be respected so long as they are compatible with fundamentals of treatment and finicking routines avoided. Milk, eggs, chicken, white fish, veal, lamb and tender meat are good if simply cooked. Frying and greasy methods of cooking make for indigestibility. Starch and sugar are allowed in moderation provided that flatulence is not a prominent symptom. Fats are given only in strict moderation. Indigestible foods such as game, cheese and butcher's offals are best omitted. Potatoes and root vegetables often disagree but purées of green vegetables may be allowed if liked. Raw salads and fruits may cause discomfort but tomato juice or pulp, citrus and pineapple juice may be given if well tolerated. Alcohol, spices, pickles and condiments may be harmful in some cases although a pre-prandial aperitif is helpful in atonic dyspepsia.

Medicines are of secondary importance to dietetic management. For indigestion with hyperchlorhydria, an antacid powder or mixture should be given in the early stages. Achlorhydric dyspepsia is rarely improved by administration of mineral acid; paradoxically alkalis are usually more effective.

Regular bowel action is encouraged by minimal doses of liquid paraffin, but purging is harmful.

Dyspepsia of nervous origin should be explained to the sufferer as such. Practical psychiatric measures, including calmatives, are indicated; the digestion receiving only incidental attention.

Gastric and Duodenal Ulcer

Systematic and prolonged medical treatment should be tried in every case of peptic ulcer. The patient's co-operation is enlisted by explaining something of the natural history of the disease and the rationale of the therapeutic measures.

Preliminary attention to the teeth, nose and throat is desirable, and any other morbid condition such as appendicular disease should have appropriate treatment.

The traditional peptic ulcer routine occupies six weeks (more or less according to severity of the condition and progress), the patient remaining in bed for the first two or three weeks. In the absence of complications he may rise daily for a warm bath and for evacuation of the bowels. Smoking and alcohol are forbidden. His mind should be freed from business and domestic cares, and as a rule this mental quiet can be best secured in hospital or nursing home. Diversional therapy in the form of reading, games or any light handwork which appeals to the patient is worth while. Apart from relief of pain, diet and medication are of minor importance by comparison with rest and relaxation.

Some authorities commence treatment of all but mild cases with a three or four days' continuous intragastric milk drip using 6 pints of milk daily with Castian, Glaxo and 1 per cent. suspension of colloidal aluminium hydroxide at the rate of fifteen drops per minute. Most patients prefer orthodox diet, but the use of a milk drip during the night (2 pints plus aluminium hydroxide suspension 1 oz.) is advantageous in

cases with persistent nocturnal pain not relieved by complete aspiration of gastric contents

Peptic ulcer diets are arranged in conformity with the following principles

- 1 High caloric value with liberal protein content and rich in vitamins to improve nutrition and encourage healing of the ulcer
- 2 Non stimulating to the gastric mucosa.
- 3 Bland to avoid mechanical trauma liquid to permit of ready buffer action with gastric secretion
- 4 Frequent regular feeds to keep the gastric juice occupied

Lenhartz diet consists of milk and eggs with rapid augmentation by sugar minced raw beef and ham It is perhaps over generous at the beginning and raw meat is unpopular

Sippy's Hurst's and Maclean's diets These have a basis of frequent milk feeds with the administration of alkalis Other bland foods are added by stages Of late the strict mushy types of diet have attracted criticism on the grounds that they do not remain in the stomach as long as more solid meals and that ulcers may remain unhealed despite their prolonged employment The following modification of Maclean's diet gives good results and is comparatively simple in practice

First week Three pints of milk daily in two-hourly feeds between 8 a.m. and 10 p.m. These should be given warm and sipped slowly Sodium citrate gr 10 is added to four feeds and the others may be flavoured with Farer Horlick's or Ovaltine Half a teaspoonful of Magnesium Trisilicate Compound Powder B.P.C. is given in water after each feed.

In the odd hours 4 oz feeds of strained gruel junket, custard or potato purée are taken followed by one half teaspoonful of Magnesium Carbonate Compound Powder B.P.C. in water

Four two-drachm doses of olive oil are given before feeds daily alternating with four doses of atropine sulphate gr 5' - (orally) A dose of trisilicate and one of atropine are given before going to sleep at night Anticholinergic drugs of the propanteline series have been used in place of atropine

for reduction of gastric acidity and relief of ulcer symptoms but a combination of atropine and phenobarbitone seems adequate for most cases. One or more feeds and some trisilicate should be placed by the bedside in case the patient awakens through the night. Active ulcers in the pyloric region may cause spasm and troublesome vomiting. Procaine is a useful remedy (20-30 ml of 5 per cent solution orally).

Whatever the type of diet used hypovitaminosis must be prevented by giving three Vitamin Capsules B P C daily.

Normal bowel movements are to be aimed at and the trisilicate or the magnesia intake should be reduced according to whether constipation or diarrhoea prevails. Occasional doses of liquid paraffin emulsion may be necessary.

Milk alkali syndrome. Patients on prolonged ulcer therapy may develop malaise, lethargy and mental confusion leading to coma. Vomiting is frequent with polyuria, hypercalcaemia, alkalosis and evidence of renal defect. Treatment is by drastic reduction of alkali base intake and sodium chloride administration by vein if necessary.

Second week. In the absence of symptoms the following are added. Two or three eggs daily as egg flip or lightly boiled. Fruit and milk jellies, cream, mashed potatoes and vegetable purees. Thin bread and butter with sieved jam or marmalade. Barley sugar, fruit drops and Turkish delight. The milk feeds are reduced in number by half and the powder reduced to six doses daily.

Third week. The following are added. Strained porridge, milk and custard puddings, steamed or boiled white fish, scraped or minced underdone roast beef, minced chicken. Sieved vegetables and fruits such as tomato, cauliflower, spinach, apple, apricot or prunes. Feeds are reduced to six during the day with milk and biscuits or sponge fingers by night if awake. Reduce the antacid to four doses a day and a night dose if required. Combinations of milk protein or glycine with aluminium hydroxide in tablet form (Nulacrin, Prodexin) are useful for after treatment. These products should be allowed to dissolve slowly in the mouth.

Fourth, fifth and sixth weeks. Add minced beef, lamb or mutton, scrambled or poached eggs, sieved root vegetables.

mild cheese plain cakes and biscuits. The atropine can usually be dispensed with at this stage.

Recurrence of symptoms is an indication for temporary simplification of the diet. The patient should be allowed up after the third week and gentle exercise in the fresh air is beneficial. Finally the diet is consolidated into four main meals with four snacks in between and sweets and chocolate (without fruit or nuts) may be taken. The oil can usually be omitted on completion of the cure and from four to six doses of powder by day and extra doses at night if awake will suffice for the average case. Iron should be given if there is evidence of anaemia (intramuscularly in the early stages a liquid oral preparation e.g. Ferromyn Elour Calmic is well tolerated later).

The risk of recrudescence of the ulcer must be impressed on the patient as well as the necessity for prolonged dietetic care.

Period opaque meal examinations and occult blood tests are desirable to confirm clinical impressions of progress. Gastroscopic examination is useful in certain cases. Re-examinations are required in cases of gastric ulcer.

Hæmatemesis. Strict rest in bed and absolute quiet are essential. Morphine gr $\frac{1}{2}$ or Papaveretum Injection B.P.C. 1 ml. should be injected subcutaneously. Two-ounce feeds of albumin water glucose solution or plain milk at hourly intervals may safely be allowed from the outset and one third normal saline flavoured with fruit juice given in quantities sufficient to relieve thirst. If bleeding persists gentle lavage of the stomach by means of a soft rubber tube will get rid of blood clots and facilitate haemostasis. When dehydration and shock have been surmounted with a modification of Meulengracht's diet should be begun.

The pulse rate and blood pressure are charted hourly. If the former rises above 120 or the latter falls below 100 a drip transfusion should be commenced without delay. The hæmoglobin level (after eight hours) is a good guide to further treatment and if it falls to 40 per cent. a litre of blood should be transfused by slow drip. If the bleeding continues several litres of blood may be required but rapid taping up is inadvisable unless immediate operation is contemplated.

After a few days freedom from hæmorrhage a full ulcer régime is instituted and iron given intramuscularly

Surgical Treatment

The question of surgical intervention arises in all cases of hæmatemesis and melæna which are not immediately responsive to the foregoing measures. Young and otherwise healthy subjects with recent dyspeptic histories are often amenable but the middle aged patient with a chronic history may well be a candidate for surgical hæmostasis. This generalisation has many exceptions however and the results of surgical intervention are now so good that there is little excuse for over long dalliance with expectant methods. A patient who needs transfusion may well require operative treatment also. Hæmorrhage complicating perforation is an indication for laparotomy.

Simple hæmostatic operations have been relegated in favour of gastrectomy and gastro-duodenectomy. Although associated with a higher operative mortality hæmorrhage is controlled with greater certainty and their long term results are superior.

Once the decision to operate has been taken an intra-venous blood-electrolyte drip should be set up to condition the patient as well as possible.

Other Indications for Surgical Treatment

1 *Chronic resistant penetrating or relapsing ulcers with severe symptoms.* Patients who are unwilling or unable to observe dietetic instructions. The nature of the operation will depend upon the lesion and the surgeon's preference.

Gastro-enterostomy. An unphysiological operation which yields excellent immediate results but the after histories are disappointing. Should be avoided if possible in younger subjects but is suitable for poor risk cases and for middle aged patients (mostly women) where gastric acidity has waned but whose symptoms are perpetuated by cicatricial pyloric stenosis.

The stoma may become ineffective or ulceration may affect the stoma or efferent loop and lead to hæmorrhage or

perforation Gastro-colic fistula is an occasional troublesome sequel.

Vagotomy with pyloroplasty or gastro-enterostomy Vagal section reduces the gastric secretion particularly the psychic and nocturnal moieties Gastric peristalsis is also inhibited so that dilatation and pyloric obstruction may be precipitated unless adequate outlet is assured On account of gradual reintegration of the gastric innervation permanent results are rarely obtained Vagotomy is contraindicated in gastric ulcer but has proved of value in cases of anastomotic ulcer following subtotal gastrectomy

Gastrectomy The operation of choice for gastric ulcer and the extent depends on the location of the ulcer With duodenectomy it is at present the most popular operation for duodenal ulcer and bleeding cases withstand it remarkably well if properly conditioned by transfusions etc

Post gastrectomy dumping syndromes of various patterns have occurred in 5-10 per cent of cases Weakness sweating and syncope are amenable to temporary alteration of the diet to include six small meals of liberal fat content daily instead of three large ones Hypoglycaemia appears two or three hours after meals Iron deficiency anaemia and macrocytic anaemia vitamin B deficiency and pulmonary tuberculosis occasionally occur as sequels of gastrectomy

2. *Acute perforation* There is still some debate as to the best method of treatment and Taylor favours conservative measures in selected cases Simple suture has a poor record as regards ulcer recurrence and further perforation Emergency gastrectomy is practised in some centres with good results in others suture is done in the first instance with elective gastrectomy later if ulcer symptoms return or radiological evidence or activity persists

3. *Chronic perforation* Operative treatment depends upon the findings, on the patient's condition and surgical resources available

4. *Flow-glass contraction of the greater curvature* is usually treated by partial gastrectomy but sleeve resection is preferred by some surgeons

5. *Pyloric obstruction* Leads to increasing gastric dilatation which necessitates surgical relief A preliminary course

of medical treatment is given but alkalis must be used sparingly as owing to the loss of chloride by vomiting alkalosis is easily precipitated. Nightly gastric lavage for seven to ten days prior to operation will allay concomitant gastritis and improve muscular tonus. Immediate pre-operative care includes a careful watch on the blood chemistry and correction of the fluid-electrolyte balance by glucose saline and potassium salts if required. Blood or plasma should be given according to indication. In chloride deficiency states normal or twice normal saline may be given intravenously until the urinary chloride output approaches 5.8 G daily. Excessive salt dosage leads to waterlogging.

Juxta pyloric gastric ulcers are difficult to cure by medical methods. Any suggestion of chronicity is an indication for surgical treatment.

6 *Ulcers where the supervision of malignancy is suspected*
Surgical treatment (usually gastrectomy) is indicated.

Gastric Carcinoma

Gastrectomy with complete dissection of the lymphatic drainage offers a reasonable prospect of cure in suitable cases. Early diagnosis is a matter of great difficulty only by submitting patients in the stage of unconfirmed clinical suspicion to exploratory laparotomy rather than to a course of alkaline therapy can satisfactory surgical results be obtained in this disease.

Total gastrectomy with oesophago jejunostomy may be followed by a dumping syndrome as well as dysphagia, regurgitation, steatorrhea and emaciation. Treatment is as described above.

For advanced cases treatment is palliative. Diet should be lightened according to the degree of discomfort present. Alkaline preparations are helpful and small amounts of morphine may be incorporated for relief of pain. Morphine, papaveretum or methadone by injection will assuredly be required later. Amiphenazole (Daptazole, Nicholas Laboratories) is a useful morphine extender (30 mg intramuscularly with each injection of morphine). Cyclizine (Marzine, B.W.) is also useful in preventing vomiting in dosage of 50 mg with each injection of morphine. Gastric

lavage is useful for persistent vomiting. Palliative surgical measures such as short circuiting gastrostomy or gastrectomy (even if metastasis has occurred) may prevent or relieve distressing symptoms. Radiotherapy is of little value.

Acute Dilatation of the Stomach

May occur as a complication of abdominal operations or in the course of severe infections. Mouth feeding should cease temporarily and glucose-salines must be given by intravenous drip, careful watch being kept on the electrolyte status. Gastric lavage and continuous suction are set up using a tranasasal Ryle's tube. Subcutaneous injections of neostigmine methylsulphate 0.52 mg at three hourly intervals may be of assistance.

DISEASES OF THE INTESTINE

Constipation

Habitual constipation may be due to dysfunction of various portions of the alimentary tract, and careful physical examination including digital and endoscopic examination of the lower bowel and inspection of the stools should be made. The patient's diagnosis is not necessarily justified and useful information can be obtained by giving a few doses of charcoal and noting the average time taken for this material to pass through the alimentary tract. Examination by opaque meal and enema may indicate the site of a hold up or confirm a diagnosis of rectal dyschezia.

Sluggish bowel habit rarely warrants the venous prognosis with which the lay mind associates it. Negative findings as regards organic disease should be communicated to the patient; reassurance and peace of mind are notable adjuncts to therapy.

In young subjects fresh air exercises such as walking, cycling, rowing, swimming, golf and gardening are helpful. In middle aged and inactive patients, mild outdoor recreations, suitable diet, remedial exercises and massage arranged to strengthen the abdominal musculature are of great assistance. Abdominal belts are a confession of failure so far as the defaecatory muscles are concerned.

Inculcation of an alarm clock habit should be the rule from earliest childhood. A call to stool on rising is the most convenient and hygienic but many require the stimulus of an after breakfast cigarette. The hour is immaterial so long as it is sedulously observed. The average water closet is designed with little regard for physiological principles but the squatting posture can be achieved reasonably well by provision of a footstool.

A liberal well mixed dietary is best and it should be made bulky by the inclusion of raw and cooked vegetables and fruits. Wholemeal porridge pre-cooked bran and wheat germ preparations are acceptable to many patients. Wholemeal bread and the various brands of crispbread have a useful cellulose content. Strong tea and coffee should be forbidden. Yoghurt and buttermilk are relished by some patients but they effect no appreciable alteration in the intestinal flora. At least three pints of fluid should be drunk daily in addition to beverages taken with meals.

Drugs have a minor rôle in the treatment of constipation except in elderly patients and immobile invalids as tolerance is quickly acquired leaving the sufferer in worse case than before. The use of mild aperients may be necessary as a temporary expedient. In cases of average severity the following remedies may be given singly in combination or in rotation.

A glass of orange tomato grapefruit or pineapple juice with early morning tea.

A helping of fruit or vegetable salad stewed prunes figs dates or apples with two meals daily.

Compound Syrup of Figs B.P.C. $\frac{1}{2}$ 2 drachms twice daily.

Confection of Senna and Sulphur B.P.C. $\frac{1}{2}$ 1 drachm twice daily.

Senokot tablets Westminster Laboratories (a standard used senna preparation) 1-4 tablets daily. More dependable than the official preparations.

Liquid Paraffin and Magnesium Hydroxide Emulsion B.P.C. 2-8 drachms daily.

Paraffin is prone to leak through the anal sphincter and by its insulating action may interfere with absorption of fats and vitamins. Methylcellulose suspensions are free from

these objections Blandart Boots (methylcellulose plus magnesia) is a representative preparation. Mucilaginous materials such as agar agar psyllium and cassia are occasionally useful as they contribute bulk and moisture to the stools.

If the foregoing measures fail temporary resort may be necessary to a wider range of aperients including effervescent salines and Sedlitz powder sodium or magnesium sulphate cascara aloes and podophyllin. The effervescent salines are very popular and in small dose are harmless. Inveterate constipated often do well on Liquid Paraffin Emulsion and Phenolphthalein B.P.C. dose 1-4 drachms.

Enemata are not desirable for routine use except in bedridden patients or as preliminary treatment of rectal dyschezia. Where the rectum is loaded with scybalous masses 6 oz. of warmed vegetable oil or liquid paraffin should be injected and retained over night the softened bowel contents are then evacuated by soap and water enema and if necessary by gentle *morcelement*. High colonic lavage is a pernicious addition the more imaginative and colon conscious types of patient should be protected from its coils. Glycerin suppositories and soap cones are for occasional use only like enemata their use tends to become a habit. Bisacodyl Dulcolax Lewis Laboratories acts as an efficient contact laxative Tablets and suppositories are available.

Spastic constipation usually co-exists with psychoneurosis. A low residue diet is best. Liquid paraffin is the only permissible laxative. Belladonna is useful in the treatment of spastic colon and may be given as gr. $\frac{1}{4}$ of dry extract in pill twice or thrice daily or it may be used in combination with phenobarbitone and ergotamine e.g. Bellergal Sandoz.

Visceroptosis requires treatment as for constipation in general. Abdominal supports and belts are sometimes helpful. Setting up exercises and massage should be ordered in correct lordotic posture.

Surgery has no place in treatment of chronic constipation, apart from relief of such conditions as haemorrhoids, anal fissure diverticulitis and organic obstruction.

Acute Enteritis

Treatment of enteritis is directed primarily to the cause. Irritative forms if seen early in the attack usually improve with a dose of castor oil. In the presence of nausea or vomiting gastric lavage should be done. Rest in bed, warmth to the abdomen and a liquid diet (fruit juice, diluted milk, albumin water and weak tea) are usually curative. Astringents e.g. Kaolin and Morphine Mixture **III P C** are less esteemed for diarrhoea than formerly but are useful for relief of pain and colic.

Codeine gr $\frac{1}{4}$ - $\frac{1}{2}$ by mouth thrice daily is helpful in the early stages.

Sulphonamides such as succinylsulphathiazole and phthalylsulphathiazole in combination with sulphadiazine are valuable therapeutic weapons for treatment of acute bowel infections particularly those caused by dysenteric organisms. Phthalylsulphathiazole should be used in initial dosage of 3 G followed by 2 G six hourly for two or three days. The broad spectrum antibiotics are superior for treatment of some intestinal infections notably those due to enteroviruses. Good results have been reported from the use of oxytetracycline (4 G in twenty four hours) for salmonella enteritis. Erythromycin and neomycin have given good results in resistant staphylococcal enteritis. Framycetin sulphate (Soframycin, Roussel) has proved as effective as neomycin in infantile gastro-enteritis due to *Esch. Coli*. Dosage 125-250 mg (50 mg/kg) daily over three to twelve days (Louette *et al* 1958).

Toxaemia, dehydration and collapse are features of severe and fulminant enteritis. reliance should be placed upon blood or plasma, glucose saline and corticosteroids by the intravenous route.

Food Poisoning

Food poisoning cases may be divided on a bacteriological basis into three groups.

Salmonella food poisoning. Contamination usually arises during preparation and storage of food stuffs. Processed meats are the commonest vehicles but milk and cream, eggs, ice cream and flour confectionery are occasionally respons-

ible Explosive outbreaks of gastro-enteritis with vomiting diarrhoea cramps and colic leading to dehydration and prostration are common Treatment is by fluid diet with codeine or Tincture of Opium B.P. for pain. A broad spectrum antibiotic such as chloramphenicol (1 G orally and then \equiv 25 G six hourly) is useful In severe cases blood plasma crystalloids and water must be given intravenously to replace deficiencies

Staphylococcal food poisoning Due to enterotoxins elaborated by coagulase positive *Staph aureus* The source is usually septic lesions of finger throat or nose of food handlers Cooked and pressed meats are frequent vehicles also milk (bovine mastitis) Sudden violent onset after an incubation period of a few hours vomiting and diarrhoea are prominent

Treatment \equiv above Erythromycin (1 G daily) \equiv efficacious and in emergency may be given by vein

Botulism. Tinned or bottled meat or vegetables (particularly home bottled vegetables) may be contaminated with spores of *Ci botulinum* The exotoxin of this organism has a curare like action weakness of the ocular pharyngeal and respiratory musculature being due to interference with acetylcholine synthesis

Treatment consists of gastric lavage purgation and early administration of polyvalent antitoxin (50 000 units daily intramuscularly) Intravenous glucose saline is occasionally necessary neostigmine methylsulphate 0.52 mg intramuscularly and repeated as necessary will control the muscular weakness The causal organism \equiv sensitive to penicillin and this remedy may have some scope in treatment particularly if the lung bases become moist

Acute Colitis

Acute catarrhal colitis may occur with acute enteritis Left abdominal colic and the passage of frequent small loose motions containing mucus and streaks of blood are common

Treatment as for enteritis Irrigation of the lower bowel with normal saline followed by a starch and opium enema (starch 4 oz. with tincture of opium 20 minims) gives considerable relief

An element of personality defect is apparent in cases of ulcerative colitis and precipitating factors such as emotional disturbance are common. Physical and mental energy is sapped with *progress of the disease* and almost inevitably the victim becomes absorbed in his colonic miseries. Formal psychotherapy is rarely acceptable but practical psychotherapy in the shape of sustained sympathetic interest on the part of the medical attendant and a patient optimistic attitude in the nurses and relatives is of great value. Outside interests must be encouraged and congenial diversional therapy arranged.

Local treatment. In general undesirable and often productive of discomfort and exhaustion. In the acute exacerbation of rectal or lower sigmoid lesions a gentle wash out with normal saline (2 pints) followed by a retention enema of starch mucilage 4 oz. with tincture of opium 20 minims will assuage colonic irritability and promote sleep. If the stools are purulent or offensive gentle colonic irrigation with normal saline is useful and may be followed by a retention enema of 8 oz. of 3 per cent. aluminium hydroxide.

Surgical treatment. Has gained favour during the past decade. It should be considered in cases which have not made satisfactory response to medical measures within a reasonable trial period and in all cases of extensive colonic damage.

Careful sigmoidoscopic and radiological examination is necessary in planning the operation. Failure is likely where the ileum is involved and a progress meal with non flocculating radio-opaque suspension will decide the point.

Ileostomy is an essential step in surgical treatment the large bowel is put at rest leading to rapid healing of the colonic lesions. With aid of the modern spigot like ileostomy opening and the Koenig Rutzen bag good control of bowel function can be quickly gained and the improvement in the patient's health is often remarkable. Restoration of bowel continuity even after several years quiescence is fraught with risk of relapse and present emphasis is therefore on colectomy which is usually done in two stages the first perhaps simultaneously with the ileostomy. In a fortunate but small minority of cases an ileoproctostomy may eventually be possible these are usually in the short history group and it

has been objected that they would probably have recovered anyway. Speculative criticism of this sort cannot detract from the excellence of surgical results in suitable cases (cachectic, toxæmic or moribund patients are not suitable).

Operative measures are imperative for such complications as acute perforation, severe hæmorrhage, perianal abscess, fistula, pseudopolyps and malignant degeneration. Arthritis of the dysenteric type and pyoderma occasionally occur and are usually considered indications for surgical treatment of the colitis.

Regional Ileitis Crohn's Disease

A chronic inflammatory condition of unknown ætiology affecting the ileum, although widespread lesions from jejunum to caecum are not rare. General measures are employed as in ulcerative colitis, to improve nutrition, combat anæmia and lessen toxæmia. Complete rest in bed is desirable when the disease is active. Diet should be bland but high in caloric value unless steatorrhœa is present; ordinary fat intake is permissible. Liquid iron and multivite preparations are given routinely and for control of diarrhœa, courses of phthalylsulphathiazole and small doses of codeine are best. Antibiotics and adsorbents like bismuth, chalk and kaolin have proved disappointing. Blood transfusion and electrolyte replacement are important and valuable contributions to therapy. Some success has attended administration of corticosteroids but experience is still meagre.

Surgical treatment is essential for refractory bowel hæmorrhage, stenosis, obstruction, perforation and fistulation. Excision is done for strictly localised disease and sometimes ileo-transverse colostomy to exclude an actively diseased loop of bowel which may be removed later. Relapse is unfortunately common.

Idiopathic Steatorrhœa Non-tropical Sprue

Has many features in common with tropical sprue: emaciation, megaloblastic anæmia (occasionally hypochromic) and steatorrhœa. Absorption of all three types of foodstuff is defective, likewise absorption of vitamins and minerals, notably calcium and iron.

Dietetic and medicinal treatment are on the lines suggested for the tropical variety. A high-calorie low fat diet is usually acceptable. a vitamin quota and iron by mouth are aids to improved nutrition. Gluten free diet has been found valuable in these conditions although response is slower than in coeliac disease. Folic acid in dosage of 5-15 mg daily by mouth helps to correct the abnormal intestinal motility pattern and will remedy megaloblastic anaemia which is common. Proteolysed liver preparations, brewer's yeast and Marmite are also valuable. For refractory hypochromic anaemia intramuscular iron (Imferon, Benger) say a course of 10 bi-weekly injections is best. Owing to increased faecal loss a potassium deficiency may arise resulting in apathy, muscular hypotonus and loss of electrocardiographic voltage replacement therapy is indicated.

Emulsifying agents have been used in malnutrition from the defective fat absorption common to sprue, steatorrhoea, coeliac disease and after certain surgical procedures such as gastrectomy, short circuiting and excision of the small bowel. Sorbitan polyoxethylene monooleates (Sorlate, Abbot, Pro-sparol, Duncan, Flockhart) are representative preparations.

Diverticulitis

This condition may produce abdominal symptoms of severity varying from constipation with colicky pain in the left lower abdomen to localised phlegmonous peritonitis. In the absence of inflammatory complications the diverticulosis is often silent. constipation is the symptom for which the patient is likely to seek advice. High residue diets cause discomfort and bland foods are indicated. The bowel contents must be kept soft by dosage with liquid paraffin before meals. Occasional oil and saline enemata are useful but aperients producing watery stools should be prohibited.

Localised peritonitis demands treatment by rest in bed, fluid diet and administration of chlortetracycline, chloramphenicol or neomycin. Resistant cases and those showing fistulous involvement of the bladder require surgical drainage, transverse colostomy is indicated for obstruction. Occasionally the affected portion of bowel is small enough to make excision and end to-end anastomosis feasible.

CHAPTER VII

DISEASES OF THE LIVER

Jaundice

There are three types of jaundice

Obstructive—following mechanical blockage of the biliary tract by impacted gall stones, pancreatic neoplasm, enlargement of lymph glands in the portal fissure etc

Toxic and infective—due to injury of the hepatic cells by chemical or organismal toxins e.g. arsenic, carbon tetrachloride, chlorpromazine, Weil's disease, infective hepatitis

Hæmatogenous—follows increased destruction of erythrocytes with liberation of excessive amounts of bile pigments e.g. Addison's anemia, malaria. Hemolytic jaundice requires no treatment other than that of the anemia.

The general treatment of jaundice is

1. Rest in bed until the skin shows little icterus and the urine is bile free

2. Diet should consist mainly of protein and carbohydrate and be liberal, varied and appetisingly served. Initial restriction of fat confers no hardship as it causes nausea and indigestion. Adequate fluid intake is essential

3. Drugs are used mostly for symptomatic indications. Alkalis and bitters may be given to allay nausea and promote appetite. Magnesium sulphate was formerly used to encourage biliary flow where stasis rather than obstruction is present. (Dosage of 1-2 drachms in concentrated solution on waking followed in twenty minutes by a tumblerful of hot water.) Bile salts are more effective and are best given in capsule form, e.g. Deubyl P.D. two thrice daily. The pruritus of obstructive jaundice can be distressing and is lessened by administration of an antihistamine such as diphenhydramine hydrochloride and application of starch or calamine lotion. Severe or persistent jaundice especially if due to chemical toxicity or hepatitis often clears under

with vitamin concentrates particularly vitamin B. Attention should be devoted to the digestive functions. Anorexia and dyspepsia are mitigated by alkalis and bitter tonics. Many cirrhotics are achlorhydric but few derive benefit from acid pepsin mixtures. Regular bowel action may be secured by nightly doses of liquid paraffin. Infections may be latent and all are potentially dangerous in hepatic cirrhosis. Active treatment should be promptly given. Sedatives particularly morphine are best avoided. paraldehyde and soluble phenobarbitone are safest.

Hæmatemesis is an alarming incident and should be dealt with as described in page 109 but morphine is avoided if possible. The dangers of excessive transfusion in this condition include dilution of circulating clotting factors increasing potential amount of bleeding into gastrointestinal tract risk of hepatic coma and citric acid intoxication. A Seng staken tube bearing a wide inflatable cuff provides direct compression of the varicose area of the lower œsophagus. A gastric balloon at the tip ensures its retention inside the cardia and effective positioning of the œsophageal cuff. gastric content can be aspirated through the tube. Obliteration of the œsophageal varices by ligature or injection of sclerosing solutions has been resorted to with doubtful results. Recurrent hæmorrhage is an indication for a shunt operation.

Hepatocellular failure may be a prominent feature and calls for bed rest liquid diet with restriction of protein according to the degree of failure as in hepatic necrosis. Nitrogen-containing medicaments are avoided and glucose vitamin infusions given. Once the mental state clears protein is cautiously restored to the diet.

Portal hypertension is a troublesome feature of some cases of hepatic cirrhosis. It may lead to ascites and œdema or to the more fatal complication of hæmatemesis from ruptured œsophageal varices. The blood protein meal subsequently absorbed from the gut gives rise to portal-systemic encephalopathy. Surgery offers substantial prospects of relief in suitable cases i.e. those in which a reasonable quantum of liver function remains jaundice ascites hepatic coma hypoproteinaemia and hypoprothrombinaemia unless reversible.

are contra indications. Various operations are used e.g. benorenal and portocaval anastomosis for extra and intra hepatic obstruction respectively.

Ascites and edema increase the patient's discomfort and must be relieved. Fluid intake is temporarily restricted, salt has already gone the way of other condiments. If the renal function is good, mersalyl 1.4 ml intramuscularly may be tried and if successful repeated at intervals of four to six days according to progress. Chlorothiazide (Salurex Merck Sharp & Dohme) is useful for control of hepatic anasarca in dosage of 1-4 0.5 G Tablets daily. Hypokalaemia must be guarded against. Intravenous dosage with salt reduced human serum albumin (50 G daily for ten days or more) is temporarily effective against anasarca in hepatic cirrhosis. If these measures fail, paracentesis should not be delayed although over frequent repetition causes undue depletion of serum proteins. Frequent change of decubitus after paracentesis will encourage mobilisation of oedema fluid from the lower limbs but multiple skin punctures or Southey's tubes may be necessary.

Cholecystitis

Acute Mild and uncomplicated attacks of gall bladder inflammation often subside under a medical regimen. Complete rest in bed is enforced and diet consists of fluids only. Sweetened fruit drinks, barley water, diluted milk and weak tea are suitable. Diet may be cautiously resumed when the force of the attack is spent. Vomiting or gastric distension should be met by an indwelling nasogastric tube, withdrawal of mouth feeding and setting up a glucose saline intravenous drip. Hot applications to the upper abdomen are useful for relief of pain, but one or more injections of morphine and atropine or pethidine may be required during the stage of activity.

Simple cholecystitis may become an immediate surgical proposition on account of suppuration, perforation or gangrene of the gall bladder. The risk of spreading peritonitis can be reduced by the use of chloramphenicol or oxytetracycline as a pre- and post-operative routine. Unless contra indication exists, the gall-bladder should be removed in a quiescent phase.

Chronic Manifests itself by nausea flatulent dyspepsia and distaste for fatty foods Pain either localised or referred with tenderness over the gall bladder area is common particularly during subacute exacerbations A characteristic history definite physical findings and cholecystographic abnormality are diagnostic but radiological evidence is not always clear-cut in the absence of stones diagnosis may be very difficult

Cholecystectomy is the only satisfactory remedy particularly if gall stones are present The following routine may be tried in patients who are unfit or unwilling for radical cure

Diet should be light and digestible Cholesterol-containing foods such as egg yolk cheese pork liver kidney sweet bread fish roes cream and suet are forbidden Lean beef lamb chicken and white fish are allowed Frying and greasy methods of cookery should be avoided Carbohydrates are harmless butter or vegetable fat may be used sparingly Vegetables often aggravate dyspepsia

Magnesium sulphate may be given in dosage just short of producing liquid stools It is taken in as little hot water as will dissolve the crystals on waking The patient lies on his right side for twenty minutes and then drinks a pint of hot water Olive or other vegetable oil (3 drachms) may be given fifteen minutes before three meals daily as a cholagogue Troublesome flatulent dyspepsia should be met by temporary restriction of diet and the administration of alkaline sedative mixtures Some patients find relief from dyspeptic symptoms by taking bile salts (dehydrocholic acid gr 4-8 in capsule thrice daily)

Gall Stones

Medical treatment aims at immediate relief of colic and alleviation of coincidental inflammation of the bile tract

For colic rest in bed and warmth to the abdomen are indicated Diet should consist of liberal quantities of bland fluids for some days after the colic has subsided Morphine gr $\frac{1}{4}$ - $\frac{1}{2}$ or Papaveretum Injection B.P.C. 1 ml with atropine gr $\frac{1}{100}$ will usually relieve the pain although a short inhalation of chloroform may be necessary until the sedative takes effect Pethidine hydrochloride 100 mg and methadone

10 mg are both effective when given into a muscle or slowly into a vein. Other suggestions are calcium chloride 2.0 ml of 5 per cent solution intravenously (slowly) papaverine sulphate gr 2-4 orally or gr $\frac{1}{2}$ subcutaneously aminophylline 0.25-0.5 G intravenously (slowly).

The patient should remain in bed until pyrexia, icterus and gall bladder tenderness have disappeared. Return to solid diet must be gradual and further management of the case is similar to that of cholecystitis.

In view of the risks associated with the ownership of gall stones, surgical treatment ought to be considered in all cases without serious contra-indication. Operation is imperative for

Severe persistent or recurrent colic, palpable or persistently tender gall bladder, prolonged or recurrent jaundice or other sign of impaction, perforation or suppuration of the gall bladder.

Pancreatic Disorders

Acute haemorrhagic pancreatitis is a rare but serious surgical emergency. Early treatment is usually non-operative: gastric suction, morphine or pethidine for relief of pain, atropine to reduce pancreatic secretion, blood and glucose saline by intravenous drip to combat dehydration and peripheral circulatory failure and antibiotics to control infection. J. G. Brooks and E. T. Jones (1956) used cortisone (300 mg daily reducing or over several weeks) as an anti-shock measure.

Recurrent pancreatitis is associated with reflux of bile into the gland due to stone in the ampulla of Vater or cholangitis with spasm of Oddi's sphincter. Such episodes may lead to pancreatic necrosis. For the acute phase conservative measures are best—gastro-duodenal aspiration, antibiotics and pethidine or atropine for pain. Laparotomy should be done in a quiet interval with exploration of the common bile duct and sphincterotomy via the duodenum.

Chronic pancreatitis syndromes are by no means clearly defined. Fibrosis of this organ occasionally follows acute infectious diseases; it may occur alone or in combination with achlorhydric gastritis and hepatic cirrhosis. Pancreatic

insufficiency may cause diabetes steatorrhœa pancreatic calculi or calcification and several of these may occur in combination

The diabetic condition calls for treatment on the usual lines For steatorrhœa dietetic regulation similar to that described for sprue is suitable and oral dosage with pancreatin should be tried Panteric Compound tablets P D contain pancreatin and bile salts

Hepatomegaly and jaundice sometimes occur in association with chronic pancreatitis and such cases are liable to be mistaken for neoplasm of the gall bladder or pancreas Surgical drainage of the gall bladder into the duodenum affords permanent relief

CHAPTER VIII

DISEASES OF THE PERITONEUM

Acute Peritonitis

This may follow haematogenous infection, injury or inflammation of the abdominal or pelvic organs or penetrating abdominal wounds. Early laparotomy is essential in most cases and a ruptured viscus should be repaired or removed. A localised appendicular abscess usually requires drainage, the appendicular stump being removed at a later date. Pneumococcal peritonitis is commonest in female children and the infection may be blood borne or from the genital tract. It responds well to combined sulphonamide and penicillin therapy but simple drainage is usually necessary as well. Gonococcal peritonitis occurs by direct spread from the Fallopian tubes and tends to localise in the pelvis. Surgical treatment can often be delayed until the inflammatory process has subsided.

Medical treatment is in general subsidiary to surgery. The patient should be propped up in Fowler's position in order to limit the inflammatory process as far as possible to the more tolerant pelvic peritoneum. Once the diagnosis is established morphine may be used in quantities sufficient to relieve pain. Aperients are contra-indicated but a small tap water enema may be ordered if necessary. Fluid by mouth should be interdicted, and glucose saline given by intravenous drip to counteract dehydration and chloride loss through vomiting. Continuous gastric or intestinal suction is useful for relief of abdominal distention.

Choice of antibiotic is governed by sensitivity of infecting organisms but parenteral administration of tetracycline or neomycin is advisable at the outset. Oral dosage is substituted as soon as the need for gastric aspiration has passed.

Gas gangrene antiserum is useful for diminution of toxæmia caused by intestinal ileus. Blood transfusion is an

excellent measure during both the early and post operative phases

Chronic Peritonitis

The localised form may follow inflammatory lesions or surgical interference. Abdominal pain and constipation are usual symptoms. Tonic measures, abdominal massage and exercises are sometimes helpful. Bowel regularity may be secured by administration of small doses of a liquid paraffin preparation.

Operative treatment is rarely beneficial except in the presence of obstructive symptoms.

Diffuse chronic peritonitis is usually a manifestation of polyserositis. Ascites is a common feature for which paracentesis is necessary. Other measures such as low sodium diet and diuretics should be tried (See p 191).

Tuberculous Peritonitis

May be primary but is more commonly secondary to tuberculous infection of mesenteric lymph nodes or a genito-urinary focus. Search should be made for tuberculous manifestations elsewhere.

The routine described for pulmonary tuberculosis is applicable. During the febrile stage complete rest in bed, a nourishing low residue diet and fresh air are indicated. Tonics of iron and fish liver oil are valuable once signs of recovery appear. Sunlight and ultra violet therapy have a good tonic effect but they must be employed with caution until individual response can be judged. Diarrhoea may be a troublesome feature which calls for temporary lightening of the diet with restriction of fats. Astringents such as chalk and opium or kaolin may be given for short periods. Constipation can be relieved by small doses of liquid paraffin. Ascitic collections require aspiration. Intestinal obstruction sometimes supervenes and surgical relief must be attempted. Abscess and fistula formation are serious complications which require surgical treatment.

Beneficial results have been reported from streptomycin employed in conjunction with the general tonic measures mentioned above. Dosage is 1 G daily intramuscularly for

the first two to four weeks and reduced to once or twice weekly when immediate objectives have been gained. PAS or isoniazid is given concurrently.

Surgical treatment apart from the complications mentioned above is in general unwise although undoubted benefit attends the removal of a localised focus e.g. Fallopian tube.

CHAPTER IX

METABOLIC DISEASES

Diabetes Mellitus

When confronted with a glycosuric patient the first step is to make certain that he is truly diabetic. In renal glycosuria the kidney threshold for glucose is lower than the usual 180 mg. per cent but the blood sugar range is normal. In the lag type of diabetes the liver storage mechanism comes into action more slowly than glucose is absorbed from the bowel and transient glycosuria appears after meals. Diabetes insipidus and pituitary diabetes connote no pancreatic defect. Transient glycosuria may occur in septic states after intra cranial lesions and in pregnancy and is not significant. Cases of renal glycosuria and those showing lag curves should be re-examined at intervals as they sometimes develop diabetes mellitus in the course of years.

The young diabetic is occasionally resentful of a regimen which is at times irksome. In justification of the therapeutic yoke (lighter though it becomes with each advance in technique) are two considerations: the phenomenal increase in life expectancy and the long term prospect of greater freedom from vascular degenerative complications such as retinitis, hypertension and nephrosclerosis in those who remain in adequate control.

Regular testing of the urine for sugar and ketones is necessary and in conjunction with blood sugar estimations at various times of the day will enable the practitioner to gauge the patient's response to treatment. A glucose tolerance test if practicable at the outset of treatment, is the best guide to the state of the patient's carbohydrate metabolism and his therapeutic requirements. The patient should have unrestricted carbohydrate for several days before a sugar tolerance test is done. The diabetic blood sugar curve will show a fasting level of over 100-130 mg. per cent. The peak

reading following 50 G of glucose by mouth will exceed 180 mg per cent after $1\frac{1}{2}$ hours instead of returning to approximately normal level the peak value is substantially maintained and after $2\frac{1}{2}$ hours the blood sugar will still exceed 150 mg per cent. If renal function is normal sugar will be found in the urine for $\frac{1}{2}$ –4 hours after the test and ketones will be present in all but mild cases. Apart from information regarding the renal threshold a single blood sugar determination two hours after 50 g glucose is equally useful.

Diabetes is a disease of infinite variety in children and young adults it is usually severe whereas in elderly, gouty and obese subjects it is often mild. Individual response is to some extent incalculable but a patient whose fasting blood sugar is around 160 mg per cent without ketonuria and with little in the way of symptoms can often be stabilised by diet alone.

The caloric value of the diet should vary according to the patient's predicted needs and obese or undernourished subjects improve on diets calculated to reduce or increase their respective weights. Obese subjects may lose their diabetic manifestations when the weight has been suitably reduced. Other factors are age, sex and surface area and in practice the adult basal requirement can be reckoned as 11.3 calories per lb body weight, i.e. a man weighing 156 lb needs 1763 calories. If however he has to expend considerable muscular energy this basic figure must be doubled (3526 cal). The protein intake should be about 0.5 g per lb body weight and so the man of 156 lb needs 78 G daily.

Carbohydrates are inefficiently oxidised in the muscular tissues in diabetes and it was formerly the practice to restrict them drastically and to make up the requisite calories by increasing the fat content. This made for unpalatability of the diet and conduced to ketosis and coma. Extended experience with insulin has shown that liberal carbohydrate allowances enhance physical and mental wellbeing and improved tolerance usually follows. It is wise therefore to give at least twice as much carbohydrate as fat.

In the example of the 1 763 cal diet

$$78 \text{ G protein} = 78 \times 4.1 = 320 \text{ cal}$$

$$190 \text{ G carbohydrate} = 190 \times 4.1 = 779$$

$$71 \text{ G fat} = 71 \times 9.3 = 660$$

1 759 cal

A selection of foodstuffs having a calorific value of 1 750 and a protein content of 78 G would be made from a Composition of Foods Table. The patient may then arrange his daily menu in accordance with seasonal availabilities by aid of a Table of Comparative Food Values.

In practice it is unnecessary to work out individual diets. A ready made one suitable in caloric content to the patient's age, size, work and diabetic condition can be adjusted in accordance with his gastronomic preferences.

There is little to be gained by starting on a low diet and working up, if the patient is otherwise healthy, much time will be saved by commencing with a diet which approximates his usual requirements. Reasonably accurate control can be maintained if the urine passed immediately before meals is tested for sugar and ketones and blood sugar estimations are done every two or three days until stabilisation has been effected (The bladder should be emptied half an hour before the before meal specimens of urine are passed). If morning fasting and before supper blood samples are taken on one occasion and on the next midday and bedtime samples a general idea of the blood sugar behaviour is obtained. In a well stabilised patient the intervals between estimations may extend to one to three months and on these occasions the before breakfast, midday and bedtime blood sugar values will indicate whether minor modifications in diet and insulin are desirable. If the renal threshold is normal and the before meal urines are consistently sugar free the intervals between blood sugar tests may be considerably longer.

The patient should if possible be up and active during the stabilisation process thus obviating the necessity for re-stabilisation later. He should be taught to weigh his diet and test the urine. Insulin recipients are taught the technique of self administration.

A patient who is inadequately controlled by dietetic regulation should be given insulin. Several types are available: ordinary soluble insulin (20, 40 and 80 units per ml), protamine zinc insulin (40 and 80 units per ml) which has a slower but prolonged action, and globin insulin (40 and 80 units per ml) the action of which is intermediate in type and which causes less local reaction than protamine insulin. Isophane insulin (NPH) is a slow action insulin containing crystalline protamine. It has many advantages including neutrality and the hypoglycaemic effect resembles a 2 : 1 soluble P : Z mixture. The protamine content is exactly covered by the insulin and soluble insulin may be safely added if necessary. We have found it suitable for most diabetics. Novo insulin (L.Z.S.) has the advantage of being protein free and rarely provokes sensitivity reactions. The buffered insulin suspension can be prepared in either amorphous form Insulin Zinc Suspension (Amorphous) (*Insulin Semilente*) which has a relatively rapid action akin to that of soluble insulin, or in crystalline form Insulin Zinc Suspension (Crystalline) (*Insulin Ultralente*) which acts for a prolonged period like protamine zinc suspension. A standard mixture of 30 per cent amorphous and 70 per cent crystalline form Insulin Zinc Suspension (*Insulin Lente*) combines the advantages of both and has an action resembling that of 5 : 1 P : Z mixtures. Novo insulins are available in strengths of 40 and 80 units per ml and are miscible in all proportions but they must not be mixed with any other type.

Ordinary insulin exerts its maximum effect in two hours and its total effect inside five hours so that it looks after one meal only. Globin insulin produces a more gradual fall in blood sugar and is active during the third to eighteenth hours after injection. The action of protamine zinc insulin is more prolonged and covers the period between the sixth and twenty fourth hour after injection. The slowly acting insulins have the advantage that after a lag of two to four hours a morning dose will influence the blood sugar curve for the remainder of the day. This depot effect is more physiological than the short lived one of soluble insulin and in suitable cases one dose daily will suffice. Their disadvantage is that if hypoglycaemia occurs it may be prolonged with

globin insulin the usual time for hypoglycaemic reactions is in the afternoon but these can be averted by allotting about 20 per cent of the daily carbohydrate allowance to the afternoon tea meal. Protamine zinc reactions are liable to occur during sleeping hours when they may go unrecognised. This dangerous possibility is avoided by reserving 20 per cent of the carbohydrate for a bedtime meal.

The following table shows the approximate distribution (per cent) of carbohydrate appropriate to various types of insulin dosage.

	Breakfast	Lunch	Afternoon Tea	Supper	Bedtime
Soluble insulin	↑35	15	7	↑35	8
Soluble + protamine	↑↓20	25	10	25	20
Insulin Lente	↓15	25	20	20	20
Isophane	↓20	30	20	30	—

Mild cases with daily insulin requirement of up to 30 units do well on any type of insulin but one dose of isophane insulin before breakfast is usually satisfactory and more convenient than a dose of soluble insulin before breakfast and supper. For cases requiring 40-100 units daily good control may be achieved with a combined dose of soluble and protamine zinc insulins before breakfast. Some severe cases respond better to two doses of globin or isophane insulin (before breakfast and afternoon tea).

Unless the patient is elderly and non ketotic it is usual to stabilise with soluble insulin and when his requirement has been gauged to substitute partly or wholly with slow acting insulin. The former is more effective against ketosis the latter gives better overall control and smaller dosage should be allowed initially. Temporary glycosuria after meals is common with slow action insulins but this may be disregarded if the blood sugar levels are satisfactory. Soluble and protamine zinc insulins should not be mixed in the syringe as the latter contains excess of retarding agent and there is risk of part of the former becoming slow acting. Double and quadruple strength insulins are a desirable refinement.

provided the patient understands the simple calculation involved.

Some improvement in the diabetic condition may be looked for after a few weeks careful treatment and this entails adjustment in diet or insulin. Moderate cases often recover sufficient carbohydrate tolerance to enable them to dispense with insulin.

Insulin sensitiveness. A few individuals become allergic to contaminant proteins and the phenomenon is more likely to appear where the use of insulin is resumed after a lengthy interruption. The patient should be tried on Lente insulin; if unsuccessful desensitisation may follow a rapid course of graduated intradermal injections commencing with 0·001 unit of insulin. Anti-histaminics are reported to be useful for this variety of allergy.

Insulin insensitiveness. Hunsworth has distinguished two types of diabetes by means of his insulin-glucose tolerance test: insulin sensitive and insulin insensitive. The former are young insulin-deficient diabetics; the latter are mostly elderly obese subjects in whom insulin over-dosage does not readily produce hypoglycaemia. Diabetes complicating other endocrine disturbances such as acromegaly and Cushing's syndrome is frequently insulin insensitive. Patients occasionally develop temporary insulin resistance for no obvious reason. Change of type of insulin should be tried.

Sulphonylureas. Non-bacteriostatic sulphonylurea products have been used to reduce the blood sugar range of mild obese and relatively recent diabetics who remain hyperglycaemic after weight reduction. The method is unsuitable for young insulin-deficient diabetics and for those with ketosis or infection. The patient should be over 40, free from complications, have a fasting blood sugar of under 300 mg per cent. and require less than 40 units of insulin daily. Tolbutamide (Orinase, Upjohn, Rastamon, Hoechst) is given orally: first day 3 G; second day 2 G; third day 1 G; and then 1·5 G daily in divided dosage after meals. Skin rashes and leucopenia have occasionally complicated

The rehydration process can be simply controlled by plasma specific gravity readings. If the blood pressure remains low concentrated plasma with noradrenaline may with advantage be added to the drip. 100-400 units of soluble insulin should be given, one half intravenously and the remainder subcutaneously and 50 units intravenously half hourly until Rothera's test becomes negative. A further subcutaneous dose of 100 units may be required if the initial blood sugar level was high (500-600 mg per cent). Warmth and quiet are essential.

As soon as swallowing power is regained $\frac{1}{2}$ oz. doses of glucose in 10 oz. water suitably flavoured are given hourly until sugar appears in the urine and ketones disappear. The blood sugar estimation is repeated when oral therapy recommences and further insulin dosage regulated accordingly. The wisdom of administering glucose to the already hyperglycaemic patient has been called in question but it can be given with safety when hypochloræmia and hæmococentration have been corrected.

During the next twenty four hours if the general condition is good the patient may be offered a light diet with 40-80 units of insulin daily in four to six divided doses. If as is often the case he is weak and tired 3 pints of milk containing 4 oz. of glucose covered by 60-80 units of insulin will tide him over the immediate recovery stage when a light diet may be substituted. After twenty four to forty-eight hours he should be ready to proceed to a standard diet at this stage further blood sugar estimations will give an indication of insulin requirements. Some return of ketonuria may attend the resumption of fixed diet but a temporary allowance of 1-2 oz. glucose will overcome this disquieting phenomenon. A careful search for inflammatory foci should be made as they are the commonest precipitating factors in diabetic coma.

Surgery in diabetes. Infections, anaesthetics and post operative starvation may induce coma in any diabetic individual. Elective anaesthesia and surgery should await control of the diabetic condition. For operations unlikely to last over two hours they should be done early in the morning if possible and no diet glucose or insulin given until the

patient has regained consciousness in severe diabetes and prolonged operations, it is customary to give 50 G of glucose by vein with 25 units of insulin subcutaneously one hour before operation. Later the patient is given the glucose value of his ordinary diet in milk and other fluids with the usual insulin allowance in four to six divided doses daily. Subsequently a light diet containing the carbohydrate value can be used until resumption of his ordinary dietetic routine becomes possible.

With regard to anesthetics, lipid soluble drugs such as chloroform, ether, Trilene and cyclopropane are unsuitable for use in diabetes and bromethol should be avoided whenever possible. Sodium thiopentone gas and oxygen, spinal and local anesthetics are safe.

Vascular degeneration is a common hazard in elderly diabetics. Renal intracapillary glomerulosclerosis gives rise to the Kummel-Wilson syndrome characterised by albuminuria, oedema, hypertension, retinopathy and gross renal function defect. Modification of the diabetic dietary to suit chronic nephritis is a matter of considerable difficulty.

Diabetes in children. The disease is more dangerous and more difficult to regulate on account of the proportionately higher and comparatively unstable metabolism of childhood. Glycogen storage is poorer than in adults and there is greater variation in physical activity. The processes of growth and maturation also make for unstable metabolism. The methods of control are the same as for adults, but carbohydrate and protein allowances must be relatively more liberal. For example in children of average build requirements are in the region of

aged four years 40 calories and 1.5 G protein per lb body weight, 130 G carbohydrate.

aged eleven years 33 calories and 1.2 G protein per lb body weight, 160 G carbohydrate.

Insulin is almost invariably required, and the combined soluble-proteamine arrangement prevents morning glycosuria and ketosis. During the course of gastro-intestinal upsets and acute infections the light diet or the sugar equivalent should be given with normal insulin dosage. Carbohydrate tolerance

usually contracts during the pubescent process and re expands afterwards. The diet and insulin prescriptions should be reviewed regularly and adjusted in accordance with progress of the disease and of growth need.

Pregnancy in diabetes. There is evidence that women in the pre-diabetic state are more prone to complications of pregnancy (particularly foetal giantism) than those who do not later develop diabetes. Treatment by insulin has greatly increased fertility in diabetic women. Pregnancy connotes a slightly increased risk to the mother's life but that to the foetus is in the region of 25 per cent despite modern methods of treatment. The increased metabolism associated with pregnancy the dangers of coma, toxæmia and sepsis and the disturbance of sugar metabolism incidental to lactation have all to be reckoned with.

Ordinary diabetic diet and insulin dosage are usually satisfactory for the first trimester of pregnancy later the protein requirement will increase to 0.75 G per lb body weight and the total calorie intake by 15-20 per cent. These may be partly provided by 2 pints of extra milk daily. Severe hyperemesis may compel temporary use of the carbohydrate or glucose equivalent and divided insulin dosage.

In addition to the routine watch on renal function daily urine tests for sugar and ketones and regular blood sugar estimations are essential.

Hydramnios and foetal overgrowth are prone to occur and there is much to be said in favour of delivery by cesarean section not later than the thirty seventh week. Infants tend to be hypoglycæmic on account of pancreatic over stimulation by maternal hyperglycæmia and early feeding with glucose may be necessary. Lactation may provoke maternal hypoglycæmia and if allowed to continue insulin dosage must be revised.

Hemochromatosis. A condition of increased iron storage in the body with deposition of hemosiderin and reactive fibrosis in liver pancreas thyroid pituitary testes and heart. Slate grey skin pigmentation hepatic cirrhosis diabetes and hypogonadism are characteristic. Increased dietary iron intravenous iron and frequent blood transfusions may lead to a similar state.

For the idiopathic variety a diet containing 100 G protein and poor in iron should be ordered. The body iron stores can be depleted by 500 ml venesections at weekly intervals until a state of mild anemia (Hb 10-11 G per 100 ml) is reached. After this infrequent venesections (1-2 litres yearly) will maintain the patient in reasonable iron balance.

Gout

The sufferer should have complete rest in bed during the acute phase. The fluid intake should reach 5-7 pints daily and the diet consist of milk, barley water, vegetable broth, soda water and fruit juice. Free bowel action is important, and a Rhubarb Compound Pill B.P.C. followed by a saline will serve. The painful limb should be elevated on pillows or light splint and pressure of bed clothes avoided by the use of a cradle. The painful joint may be bandaged lightly with cotton wool but alkaline fomentations, evaporating lotions or kaolin poultice are preferred by some victims. Physiotherapeutic methods such as massage, radiant heat and short wave diathermy are best omitted.

Colchicum is a traditional remedy and Colchicum and Sodium Salicylate Mixture B.P.C. may be taken three hourly until relief is obtained.

Prolonged use of this drug is liable to provoke diarrhoea. Colchicine is more reliable in action than the galenical preparations. Dosage of 0.5 mg every hour or 1 mg two-hourly should be continued until pain disappears or diarrhoea supervenes. In subsequent attacks the dose just short of causing intestinal irritation may be reached rapidly with correspondingly early relief. If severe diarrhoea results it is controllable by tincture of opium in minimum doses. Salicylates have some effect in promoting uric acid excretion but they are rarely satisfactory as analgesics in the acute phase and a subcutaneous injection of morphine or methadone 10 mg intramuscularly may be desirable at the outset of treatment. Phenylbutazone (Butazolidin Geigy) 200 mg six hourly for 8-10 doses is effective in treatment of acute gout. ACTH 5-1 (100 units intramuscularly) and prednisone (40 mg daily orally) have been used alone or in combination with colchicine or phenylbutazone.

For *interval treatment* a hygienic mode of life should be enjoined with attention to such details as avoidance of chill moderate daily exercise and regular bowel elimination Obesity if present call for correction and concomitant conditions like arthritis diabetes and arteriosclerosis should have adequate treatment Alcohol and purin-containing beverages are interdicted Over indulgence in flesh foods is harmful and it was customary to proscribe the following liver sweetbread kidney sardines herrings fish toe game soups and sauces made from meat stock rhubarb spinach watercress mushrooms peas and beans Diminution of fat intake with increase of carbohydrate tends to reduce the frequency of attacks Blood fluid and alkaline waters may be drunk freely and they acquire additional merit when taken as part of a spa routine

Salicylates *diminish reabsorption of uric acid in the renal tubule* and by lowering blood uric acid levels in chronic gout the patient's condition is improved and acute attacks reduced in frequency and severity Sodium salicylate gr 80 may be given daily for several months together with a vitamin B preparation Colchicine (0.5 mg. once or twice daily) and probenecid (0.5 G. twice or thrice daily) are excellent in combination for interval treatment of cases showing frequent or severe attacks The lowest effective dosage should be maintained over years until the gritty tendency has waned Uricosuric agent should be used cautiously in patients with a tendency to urate stone formation

Obesity

The influence of heredity age race and endocrine activity is important and uncontrollable but by ceaseless attention to diet and exercise the patient can do much to neutralise their effect The only proven cause of obesity is excessive food intake Gluttony is often a solace against an unsatisfactory milieu the individual who is unfortunate in love at games or in the occupational sphere can at least become a notable trencherman There is also the persistent fiction that obesity is synonymous with serenity good cheer and dependability

Alcohol should be forbidden in all cases of obesity. Some sufferers consume large quantities of water and/or salt for these strict limitation of intake must be practised. Mild and early cases do well on a dietetic regime in which protein and inert foods are substantially increased with corresponding reduction of fat and carbohydrate.

Grossly overweight subjects benefit from a course of inpatient treatment. They should be made aware of the poor life expectancy associated with the disease. Psychological insight and re motivation towards an attractive figure and satisfactory health status should be encouraged to ensure the patient's active co-operation. The first few days are spent in bed and a fast diet given. This consists of one grapefruit or two oranges, water, weak tea and coffee with milk and saccharin, vegetable or meat broth, jellies made with gelatin and saccharin, shredded lettuce or cabbage, cress or other green vegetable with mineral oil and vinegar dressing. A weighed low calorie diet is then allowed for four days per os with a fast day between. Another successful hospital routine is the 600 c. 200 c. diet on alternate days.

Thyroid extract is a traditional remedy but one of doubtful efficacy. The commencing dosage may be gr. 1 daily cautiously increased to gr. 3. In resistant cases progress can often be initiated by the exhibition of mercurial diuretics and ammonium chloride. In the absence of contra indications 4 ml. of mersalyl may be given intramuscularly twice weekly for six doses with coverage of ammonium chloride.

When a satisfactory weight loss has been recorded, the patient is discharged on a low calorie diet with which he must be content until the adipose tendency is lost—often a matter of years. Many find a weekly fast day a useful corrective and it need not be spent in bed. Thyroid feeding may be continued in moderate dosage if required, but the patient should not be allowed to regard it as a substitute for dietetic austerity. Dexanphetamine sulphate is useful for dulling the pangs of appetite and promoting euphoria and is generally preferable to thyroid extract. The dose is 25.5 mg. before breakfast at 11 a.m. and at 4 p.m. Preludin Pfizer acts similarly but has no hypertensive effect. Dose one 25 mg. tablet before breakfast and lunch.

Open air exercise is an important detail of treatment although markedly inferior to dietary regulation as an aid to weight loss. It has been brought to a fine art by professional weight losers such as jockeys and pugilists. Walking, golf, tennis, squash, racquets, swimming, gardening, football and soft ball are excellent. Massage and remedial exercises restore muscle tone and improve peripheral circulation although fat cannot be massaged away.

CHAPTER X

DISEASES OF THE DUCTLESS GLANDS

THYROID GLAND

Simple Goitre

In areas where the condition is endemic the prophylactic administration of small quantities of iodine to children and expectant mothers has given good results. The dose need not exceed gr $\frac{1}{2}$ of sodium iodide daily for periods of ten weeks during the spring and autumn. The use of iodised table salt is a convenient method of dosing the whole population (5-10 mg. potassium iodide per kg. of salt). Thyroid enlargement of puberty and pregnancy should as a rule be left alone. Diffuse goitre of short duration sometimes disappears under treatment by thyroid extract gr 1-3 daily.

Operation is advisable for large and long standing goitres for those showing nodules and for cosmetic or psychological reasons. The advent of pressure symptoms, thyrotoxicosis or neoplastic change calls for surgical treatment.

Drug induced goitre (para aminosalicylic acid, sulphonamides, resorcin by local application) disappears when the offending drug is excluded.

Hyperthyroidism Exophthalmic Goitre

The acutely thyrotoxic patient should have complete rest in bed in a cool, quiet and well ventilated room. Mental serenity and freedom from everyday vexations are best ensured by treatment in hospital. The tendency to excitability should be subdued by administration of phenobarbitone gr 1-3 daily or an evening dose of a suitable hypnotic e.g. chloral hydrate gr 10 butobarbitone gr 1½-3 may be added for obstinate insomnia.

Thyrotoxic subjects are often undernourished and a high calorie diet is desirable. A negative calcium and iron balance

is common, and may be corrected by calcium salts vitamin D concentrates and an acceptable iron preparation.

Infective foci have an aggravating influence and likely sources of sepsis should be investigated. Small foci such as dental abscess or maxillary sinusitis may receive treatment but more ambitious projects like dental clearance or tonsillectomy must be deferred until the thyrotoxic condition has been dealt with. Similarly complications such as auricular fibrillation and diabetes are given temporary treatment as adequate control is impossible until the thyroid overactivity has been restrained.

Antithyroid drugs The thiourea group reduce thyroid activity by inhibiting the synthesis of thyroxine. Thiouracil will usually bring the metabolic rate to normal within a few weeks but the goitre is likely to remain or enlarge and exophthalmos is but slowly relieved or increased. These unpleasant possibilities are unlikely if thyroid extract gr 2-4 daily is given simultaneously. Dosage is in the region of 100-150 mg three daily until the basal metabolic rate has regained normal level. The intake is then reduced to 50-100 mg daily. With all antithyroid medication a minimal maintenance dose may be necessary over months or years. Pulse and weight records should be kept and the optimum dose is that on which the pulse rate is maintained m 70-80 and normal weight regained. If the initial dosage is unnecessarily prolonged myxoedema and thyroid hypertrophy mediated by the anterior pituitary thyrotrophic hormone will result. Relapse or recurrence is an indication for increase in dosage or retreatment. Thrombocyte and leucocyte counts are necessary at regular intervals as these drugs are potentially toxic and neutropenia may develop suddenly despite regular haematological control. Medication should be discontinued immediately if the leucocyte count falls below 3 000 per cumm or if fever sore mouth or throat vomiting or skin rash appear. Patients should be warned to report such symptoms immediately. Toxic jaundice is a rare complication.

Methylthiouracil is active in slightly smaller dosage cheaper and generally less toxic than thiouracil. 6-n propyl thiouracil is still less toxic and effective in smaller amounts (initial dosage 150-300 mg daily maintenance 50-75 mg.)

Carbimazole (Neo-Mercazole Schering) is the least toxic and most active and dependable of all antithyroid presently available. Initial dosage is 15-45 mg. (3-9 tablets) daily for two to three weeks according to severity of symptoms. Subsequently reduction can usually be made to 10-20 mg. daily until the thyrotoxic manifestations have come under control. maintenance therapy lies in the 2.5-15 mg. region.

Psychotics require a long pre-operative routine as do thyrotoxic cases complicated by pregnancy. Operation may safely be done in the first four months of pregnancy but carbimazole is the method of choice for patients seeking treatment at a later stage. The drug should however be replaced by iodine during the last month of pregnancy otherwise foetal goitre may occur.

Surgical treatment. In expert hands subtotal thyroidectomy gives excellent results with a mortality of under 1 per cent. In the antithyroid drugs the surgeon has valuable allies in the shape of substances which will act with certainty as pre-operative metabolic stabilisers. by their aid almost every desperate surgical risk case can be converted to a normal risk.

Pre-operative treatment. For all but the mildest cases the routine of rest, liberal diet and two to four weeks carbimazole therapy is initiated, not necessarily in hospital. When the metabolic rate has fallen to normal this is replaced by Lugol's iodine 10 drops in milk thrice daily or potassium iodide 125 mg. thrice daily for ten days. The abnormal vascularity of antithyroid treated goitres increases the technical difficulties of the operation but interval treatment with iodine overcomes this objection.

Thyrotoxic crisis. May present in severe cases or (rarely) complicate the immediate post-operative stage. Unrecognised the mortality is high. Various types have been described but there is no sharp distinction. Hyperpyrexia, vomiting and diarrhoea, emaciation, maniacal delirium and confusional psychosis ending in apathy and coma are common. Prompt treatment is important. Hyperpyrexia is met by removing the bed-covers and applying a damp sheet on which a fan plays. Ibibation by ice packs or cooling coils is better for

vomiting and diarrhoea mouth feeding is suspended in favour of intravenous glucose saline with blood or plasma if required and salts as necessary to maintain electrolyte balance Cardiovascular manifestations (auricular fibrillation or flutter paroxysmal tachycardia) require appropriate remedies Agitative psychoses are controllable by hydrotherapy and hibernation cocktail (chlorpromazine 33 mg promethazine 10 mg and phenobarbitone gr 1) three or four times daily General therapy of the thyrocritical state includes high caloric intake liberal vitamin supplements ample fluids and Aqueous Solution of Iodine B.P. 2 ml in 560 ml 5 per cent glucose intravenously six hourly oxygen inhalations to combat cerebral hypoxia and cortisone 100-200 mg orally or hydrocortisone 100 mg intravenously Antithyroid drugs are too slow in action to affect the immediate crisis but the outlook is improved by large dosage (carbimazole 100 mg and 30 mg six hourly for twenty four hours then 30 to 60 mg daily until thyrotoxicosis is controlled) Aqueous Solution of Iodine is usually given also (0.5 l ml in milk six hourly for forty-eight hours)

Surgery With efficient preliminary medical treatment surgery gives a quick and aesthetically satisfactory cure with small operative mortality and relapse rates although tetany and laryngeal paresis are occasional complications Anti-thyroid agents are not so uniformly effective in male subjects and are markedly inferior to surgery against secondary thyrotoxicosis Surgery lessens the risk of future thyroid neoplasm and is the treatment of choice in retrosternal goitre where further thyroid enlargement might prove fatal

Radiotherapy Deep therapy is now little used except in cases considered unsuitable for other measures Radioactive iodine (^{131}I) yields excellent results in diffuse hyperplastic toxic goitres but its action is slower and less predictable in toxic adenoma It is probably the treatment of choice for recurrent thyrotoxicosis after surgery Some workers confine radioiodine therapy to patients over the age of fifty on account of the possible risks of carcinogenesis renal and gonadal damage Ordinary iodine and antithyroid drugs must be omitted for six weeks before embarking on this treatment The average dose necessary to induce remission is 0.05-0.15

mc per G of thyroid tissue. The gland weight is estimated clinically: the average figure is about 56 G and large glands weigh about 150 G. Dosage depends on gland size rather than degree of toxicity and is usually in the region of 6-10 mc orally. If necessary a further half-dose is given after four months: a third is rarely required. The risks associated with this method of treatment are hypothyroidism and glandular carcinoma (speculative).

Exophthalmic Ophthalmoplegia

A troublesome complication of thyrotoxicosis characterized by exophthalmos (often masked) thickening and oedema of the eyelids chemosis and extra-ocular paralyses. It may arise in a hyperthyroid subject rendered euthyroid by one or other of the measures outlined above and may present in an aggravated form in patients who have only slight thyrotoxicosis. The condition is caused by excessive production of pituitary thyrotrophin. Thyroidectomy normal antithyroid medication and radiiodine will produce rapid worsening of the eye signs especially if the metabolic rate is lowered rapidly. Thyroid extract in large dosage inhibits thyrotrophic activity and shows a mild diuretic action also: this should be reinforced by salt and water restriction and acetazolamide. Cortisone or delta-cortisone has been used with success in cases of rapid onset (prednisone 20-40 mg orally daily for two weeks). The eyes should be protected from dust and wind by glasses and the patient should sleep with the head elevated. Chemosis causing conjunctival herniation and corneal ulceration are indications for lid suture. Threatened visual loss is met by orbital decompression. Irradiation of the post-orbital regions has been recommended.

Hypothyroidism Myxœdema

Undue susceptibility to cold is common and the patient should be warmed up and kept warm. Thyroid extract is an invaluable remedy but it must be continued for the remainder of the patient's life. The optimum dose is ascertained by experiment and it is wise to begin with gr 1 daily and increase by gr $\frac{1}{2}$ at monthly intervals. Dosage exceeding

gr 3 is rarely necessary. A gradual increase in the pulse rate to normal with steady fall in body weight and increase in mental and physical responsiveness are to be aimed at. Large initial dosage may be dangerous and elderly subjects and those with cardiovascular lesions should be kept on sub-optimal intake until the myocardial reaction can be ascertained. Thyroid rapidly increases the demand on the myxœdematous heart but improvement in myocardial nutrition comes more tardily. Over zealous therapy may thus precipitate myocardial infarction.

Synthetic l thyroxine sodium is of uniform potency and may be substituted for thyroid extract. 0.1 mg. of the former is equivalent to gr. 1 of the latter.

Anæmia may be hypochromic, megalocytic or macrocytic in type. The first responds to iron, the second to liver or vitamin B₁₂, and the last responds (slowly) to thyroid extract. Eventually all types tend to become responsive only to thyroid.

L-triiodothyronine (Tertroxin, Glaxo) is the form in which thyroid hormone acts in the tissues. Its position in therapy of hypothyroidism is not yet settled but it seems to be valuable in treatment of two severe hypothyroid states—myxœdema madness and myxœdema coma. In the former dosage of this very active agent up to 0.1 mg. (equalling gr. 5 of dried thyroid) daily has been suggested. The obstinate hypothermia associated with coma calls for gradual warming up of the body, intravenous glucose saline, liberal dosage with delta-cortisone to correct adrenal cortical hypofunction and triiodothyronine (to a total of 0.2 mg.).

Hashimoto's struma. These patients tend to become myxœdematous particularly after surgery. Thyroid extract gr. 3-5 daily is the best remedy and should be continued for many months if required. Radiation of large goitres is sometimes necessary as well but operative measures should be conservative and to relieve compression.

Cretinism

Endemic cretinism is found in goitrous areas but the disease occurs sporadically. It may go unrecognised during the first eighteen months of life. As early and adequate

treatment ■ essential for complete mental and physical development the practitioner should form a mental picture of the infant cretin rather than of the full blown child cretin in whom the mental response rarely parallels the physical response to thyroid treatment Hypothyroidism may be suspected in infants of two months and upwards who show pallor with dryness and inelasticity of the skin They are often unusually placid somnolent and constipated and may be lazy feeders The abdomen becomes distended and umbilical hernia is frequent

Substitution therapy must be given for the remainder of the patient's life The initial dose of thyroid extract should be pushed to toxic levels and then reduced slightly but increased in proportion to growth (two to four months gr $\frac{1}{2}$ four to eight months gr $\frac{1}{4}$ eight to twelve months gr $\frac{1}{2}$ two years gr $\frac{1}{2}$ 1½ four to twelve years gr 1-3) Individual dosage varies according to tolerance and progress but it should always be just below the toxic level

Childhood myxedema May arise as a sequel to infectious or other illness in a subject whose thyroid is hypoplastic Supplementary thyroid therapy is required and over a smaller range of dosage than in cretinism Commencing dose should be gr $\frac{1}{4}$ daily and increased gradually Loss of weight and return of vivacity and energy are indicative of adequate treatment Normal skeletal development (assessed radiologically) is a useful objective criterion

PARATHYROID GLANDS

Tetany

Caused by hypofunction or removal of the parathyroid glands Some disturbance of calcium metabolism is always present and usually a diminution of serum calcium

Tetany following removal of a parathyroid adenoma may be relieved by intravenous injection of 10-20 ml. of 20 per cent calcium gluconate solution intravenously A diet low in phosphorus, with calcium lactate 20 G daily by mouth will enable the patient to become tolerant of his parathyroid deficiency

Cachexia strumipriva Follows extirpation of the parathyroids and its manifestations may be severe. Immediate signs of hypocalcemia are abolished by the administration of 20 ml of 20 per cent calcium gluconate solution slowly into a vein. This may require repetition in three hours. Parathormone quickly becomes ineffective. Continuation treatment consists of calcium gluconate 8 G thrice daily with vitamin D 25 000-100 000 units daily or A T 10 2.5 ml weekly or twice weekly by mouth. Serum calcium estimations are necessary during the first weeks of treatment later. Sulkowich's test for urinary calcium will provide convenient control of calcium balance. The intake of foodstuffs rich in phosphorus should in theory be reduced but as milk is a good source of calcium also little is gained by excluding it. In practice dietetic restriction is omitted and a positive calcium balance maintained by continuing with calcium gluconate (or lactate) in dosage of 20 G daily together with calciferol or A T 10. Calcium absorption can be improved by giving 2-4 drachms of dilute hydrochloric acid or gr 90 of ammonium chloride daily. Phosphate absorption is depressed by liberal dosage with aluminium hydroxide (Aluminium Hydroxide Tablets B.P.C. 6-12 daily).

If the condition arises after thyroidectomy the patient may be hypothyroid as well in which case thyroid medication will lessen both deficiencies. Parathyroid grafts have proved successful.

Tetany associated with alkalosis may be provoked by overdosage with alkalis by prolonged vomiting or overbreathing. Tetany may complicate the crises of Addison's disease and hypokalemia. Treatment must be directed primarily to the cause and the symptoms can be relieved by administration of calcium and ammonium chloride. In cases due to persistent vomiting resort must be had to intravenous calcium (gluconate 40 ml of 20 per cent solution chloride 20 ml of 5 per cent solution) followed by normal saline to redress the plasma electrolyte balance.

Tetany due to vitamin D deficiency occurs in rickets and coeliac disease. In the former condition tetany may be precipitated by the inauguration of vitamin D therapy. Spasmodic manifestations are met by intravenous injection of

5-10 ml. calcium gluconate solution followed by mouth dosage with calcium chloride gr 40-60 daily for several days. When the tetanic signs have abated a vitamin D concentrate should be prescribed in dosage of 8 000-12 000 units daily together with a general antirachitic routine. Dihydrotachysterol (A T 10 Bayer) produces marked increase in calcium absorption and phosphorus excretion. It may be used in dosage of up to 3 ml. daily orally in place of calciferol in tetanic states other than those complicating rickets. It is not antirachitic.

Hyperparathyroidism

Generalised fibrocystic osteitis is usually due to the activity of a parathyroid adenoma. Serum calcium and urinary calcium are increased, serum phosphorus is reduced and the serum alkaline phosphatase increased. Urinary calculi are frequent. Surgical exploration of the parathyroids is indicated. Unfortunately the adenoma may be difficult to locate on account of its small size or situation in a mediastinal parathyroid rest. Simple hyperplasia accounts for some cases of hyperparathyroidism and relief follows removal of two or three parathyroids. The pre-operative routine includes a diet poor in calcium and phosphorus with liberal fluid intake to protect the kidneys. Intractable tetany may follow operation as available calcium is sucked into the softened bones. Calciferol and A T 10 are not effective. liberal intravenous calcium is required for several weeks (100-200 ml. of 10 per cent calcium gluconate in 5 per cent glucose by slow drip daily).

Hyperparathyroidism may complicate chronic renal disease with acidosis in which case the serum calcium is generally low or normal. Treatment consists of a citric acid sodium citrate mixture to overcome the acidosis plus calcium gluconate and calciferol (15 G. and 50 000 units daily).

PITUITARY GLAND

Posterior lobe deficiency. Diabetes insipidus arises from defective functioning of this organ but the relationship is a complex one in which the anterior lobe infundibulum

and the tuber cinereum play a part. The condition may follow injury or inflammation involving the base of the brain, tumours involving the third ventricle or lesions of the hypothalamus. The presence of syphilis should be excluded.

The disease is in itself harmless apart from the discomfort incidental to polydipsia and polyuria. Treatment is by administration of pituitary antidiuretic hormone and is not successful in every case. Posterior pituitary extract may be snuffed in powder form (40 mg. three daily or 0.25-0.5 ml. of pitressin sprayed intranasally from an atomiser) but injection is as a rule more effective. Pitressin tannate in oil (1 ml. = 5 pressor units) may be given into a muscle at intervals of two to four days. Dose 0.4-1 ml. Overdosage with antidiuretic hormone will lead to water intoxication. Cases due to intracranial compression should receive appropriate surgical treatment.

Anterior lobe. Gigantism and acromegaly are due to eosinophil adenoma (usually benign) of the anterior pituitary and oversecretion of growth hormone. The former condition is found in children while the latter arises after puberty. Cushing reported the beneficial effect of radiotherapy in gigantism. Extirpation of an eosinophil adenoma is possible in some cases of acromegaly; in others radiotherapy may be given trial. Rapidly growing tumours causing loss of vision are unsuitable for radiation and surgery is preferable. Oestrogens in large dosage (combined with testosterone in male adults) may retard the osseous overgrowth. Hyperthyroidism, diabetes and post-operative hypopituitarism should have appropriate treatment.

Chromophobe adenomata give rise to no specific effects. They cause pressure atrophy of adjacent chromophil cells and the patient ultimately develops panhypopituitarism. Surgical removal is best. Basophil adenomata are responsible for the appearance of Cushing's disease; a similar syndrome may originate from an adrenal cortical tumour. Surgical removal is rarely feasible but radiotherapy may be helpful.

Anterior pituitary hypofunction. Gives rise to various types of infantilism. If the deficiency is congenital a state of

pituitary dwarfism occurs arising in later childhood after infectious diseases or intracranial compression e.g. from chromophobe adenoma the Lorrain Levi syndrome results (gonadal hypoplasia with dwarfism)

Growth hormone preparations are ineffective in man but administration of androgens at puberty usually induces growth and epiphyseal union with virility and muscular development. In females the same régime is applicable with small doses of stilboestrol. Thyroid and cortisone should not be used in the absence of specific indication. Alternating courses of oestrogen and progesterone are useful during the post pubertal phase in females.

Simmonds disease. Due to infarction and atrophy of the anterior pituitary consequent on severe illness such as post partum hæmorrhage sepsis or pressure from a parapituitary tumour. Vascular occlusion and tumours account for over 90 per cent. of cases.

Those originating from intracranial compression require surgical relief. Mild examples following obstetrical shock may improve or recover with the pituitary hyperplasia incidental to a subsequent normal gestation. Pituitary hormones have in the main proved useless but many cases show satisfactory response to replacement of the secondary deficiencies—gonadal, thyroid and adrenal. Thyroid extract gr. 1 daily should be given only to cases already on cortisone otherwise Addisonian crisis may be precipitated. Cortisone is of great utility and should be given in dosage of 15-40 mg. orally daily slowly reduced to a permanent basal intake of 5-15 mg. Prednisone and prednisolone are equally useful in about one fifth of this dosage. Testosterone should be given to both sexes—as methyl testosterone 10 mg. sublingually daily or as subcutaneous implants of testosterone (females two or three pellets of 75 mg. males twice this amount). Hirsutism is an advantage in men but in women it must be avoided by careful dosage. Intercurrent infections may lead to coma and should have prompt treatment including increased cortisone. Anæsthetics, hypnotics and insulin are potentially dangerous.

Frühlich's syndrome. The main features are dwarfism and obesity with lack of sexual maturation. It is commonly

caused by pressure of a craniopharyngioma and improvement follows operative relief. Gonadotrophic hormone and thyroid extract may be tried but many cases in this group improve spontaneously.

Hypopituitary coma Induced by physical or mental strain, infection and other acute illness. The patient may show hypoglycæmia, hyponatræmia, hypotension and hypothermia; water intoxication is frequent. Treatment is firstly directed to the precipitating cause and intravenous hydrocortisone is of great assistance in all cases, both in prevention and cure (hydrocortisone) 50-200 mg. by vein repeated as necessary. Intravenous glucose is generally valuable also saline to combat overhydration. Hypothermia responds to warming methods (hot bath or hot air bath). Thyroxine and DCA are indicated in some cases.

ADRENAL GLANDS

Cushing's syndrome May originate from a neoplasm of the pituitary basophil element (Cushing's disease) or from a simple or malignant tumour of the adrenal cortex (Cushing's syndrome). One case in three shows adrenal hyperplasia but degenerative pituitary change not infrequently accompanies adrenal tumour. Cushing's syndrome with isolated adrenal abnormality is rare in males.

Whatever the morbid anatomy, clinical characteristics are predominantly those of overproduction of adrenal corticosteroids. They include metabolic disturbances such as obesity, hypertension, diabetes and osteoporosis. Muscular weakness and atrophy, striæ distensæ, acne hirsutæ, hypokalaemia and hypochloræmic acidosis are common. Sexual and skeletal development are often precocious in children and females develop on heterosexual lines, i.e. male muscle and hair distribution, enlarged clitoris. Adult females tend to acquire male characteristics and amenorrhœa, whereas males may become feminised with gynæcomastia and impotence.

Treatment depends on the findings. Adrenal exploration is indicated in cases of extra pituitary origin although the tumour may be elusive or of an infiltrating type which makes removal difficult. Sprague recommends that if a tumour is

found in the gland first explored it should be removed. If the gland is atrophic the tumour is probably in the other adrenal. If the gland appears normal 90 per cent is removed and the other gland explored. If this is normal or hypertrophied it should be removed. Adrenal exploration may be done in two stages if the patient's condition so requires. Since the function of the contralateral gland is depressed by an adrenal tumour severe deficiency will arise post-operatively. This is countered by administration of cortisone intramuscularly 200 mg. daily by divided dosage on the three pre-operative days. Post-operative dosage is on average 100 mg. intramuscularly daily for three to four days and then gradually reduced. A maintenance dose of cortisone or dethacortisone orally is necessary in some cases. Post-operative acidosis and hypokalaemia are treated by oral potassium chloride 2.1 G three daily.

Congenital or acquired adrenocortical hyperplasia causes virilism. Arising before the fourth month of fetal life pseudohermaphroditism occurs in females and macrogenitosomia praecox in males. Arising later hirsutism and clitoral hypertrophy occur. The 17 ketosteroid excretion is much increased. Cortisone orally or intramuscularly relieves the condition by inhibiting secretion of corticotrophin.

Aldosterone. An adrenal cortical steroid identified by S. A. Simpson and colleagues (1952). It has since been crystallised and synthesised. It is 30-100 times as potent as DCX in controlling renal sodium and potassium loss. In Addison's disease the aldosterone elaborating cells perish but are intact in hypopituitary states. J. W. Conn (1955) described the syndrome of primary aldosteronism due to adrenal tumour consisting of increased urinary output of the steroid, hypokalaemia, nephropathy, hypertension, tetany, muscular weakness and periodic paralysis (including cases formerly diagnosed as potassium-losing nephritis). These are cured by removal of the adrenal tumour. Other cases presumably secondary show sodium retention, ascites and oedema.

Adrenal cortical deficiency. The acute form is known as the Waterhouse-Friderichsen syndrome. It occasionally results from adrenal infarction or injury but more commonly follows adrenal haemorrhage in fulminating infections such

as meningitis and pneumonia. Clinically it presents as an intense shock state with extensive purpuric rash and cyanosis. Anti shock measures should be instituted (maintain body warmth raise foot of bed set up plasma transfusion) Morphine should not be used. Give 1 noradrenaline in glucose saline drip intravenously or better hydrocortisone 100-150 mg in glucose saline 500 ml over three to four hours or hydrocortisone hemisuccinate (Ef Cortelan Glaxo) 100 mg in 2 ml water slowly intravenously. In infective cases prompt and effective antibiotic therapy is essential.

Addison's disease. Due to bilateral destructive lesions of the adrenal cortex. Some cases are caused by fibrosis following tuberculous infection, simple atrophy accounts for many. Sodium and water are lost while potassium is retained.

Treatment is directed to increasing the sodium content of the tissues and substituting for the deficient hormone. Sodium chloride in dosage of 2.5 G daily will improve the patient's condition and lessen his hormonal replacement requirement especially if no DCA is given. Its irritant effect on the gastric mucosa can be minimised by using 1 G enteric coated tablets or by distributing the salt in suitable foods and fruit drinks. A diet of the high protein high calorie type is suitable. Carbohydrate snacks prevent hypoglycaemic incidents.

Replacement by cortisone or its analogues is essential therapy in Addison's disease. Maintenance requirements vary widely but a start may be made with cortisone 15-50 mg (prednisone or prednisolone 3-10 mg) orally daily by divided dosage. Although inadequate alone a background of DCA (desoxycorticosterone) seems to make some patients feel and do better. It is preferably given as pellets of fused crystals implanted into the subcutaneous fat of the abdominal wall (75-150 mg). This remains active for six to eight months. The trimethylacetate suspension intramuscularly is active for one month (dose 30-60 mg). During any period of special stress the allowance of cortisone must be increased. During intercurrent illness of infective nature the increase must be three or four fold and adequate antibiotic therapy given as well. Otherwise the patient is liable to go into Addisonian crisis.

The criteria of successful regulation of Addison's disease are gain in weight, appetite and energy, elevation of blood pressure and restitution of normal sodium, potassium, glucose and urea levels in the blood. The patient should remain in bed until a satisfactory gain in weight and energy materialise and he should be protected from cold. Vomiting and diarrhoea are met by temporary restriction of diet. Fluids, alkalis, sedatives and astringents may help. Purgatives are forbidden. Search should be made for tuberculous foci particularly in the chest and genito-urinary system. Overdosage with cortisone or DCA will cause hyperchloremia, azotemia, generalised oedema and consequent cardiac embarrassment.

Addisonian crisis. Absolute rest in bed is necessary with prompt treatment of any coincident infection. Intravenous saline (5 per cent.) with glucose must be given by drip infusion. Hydrocortisone 100-150 mg. should be added to the drip or Ef-Cortelan Glaxo 100 mg. dissolved in 2-10 ml. of saline and given slowly intravenously. These may be repeated as necessary at eight hourly intervals until mouth dosage becomes effective. Cortisone acetate 100 mg. into a muscle and repeated in half dosage every eight hours is very useful intermediate therapy in severe cases. Further saline and fluid infusion should be controlled by laboratory data to avoid overhydration. unresponsive shock and hypotension call for the addition of 1 noradrenaline 4 mg. per litre of saline. Once the patient is able to resume feeding, the routine described for Addison's disease should be put in train.

Phaeochromocytoma. Tumours arising from chromaffin cells of the adrenal medulla which induce hypertension by virtue of their adrenaline or noradrenaline content. They may be multiple and are sometimes located in aberrant medullary tissue. The hypertension may be paroxysmal with symptoms of hyperadrenalism: i.e. giddiness, palpitation, headache, dyspnoea and syncope or sustained.

Removal of the tumour is curative. Handling causes a dramatic hypertensive response and post-operative hypotension is equally dangerous. For the acute hypertension phentolamine (Regitin, Ciba) is added to a saline intravenous drip in amounts of 5 mg. as required when the

diastolic pressure exceeds 140 mm. Serious fall in blood pressure is likely after ligation of the veins and a 0.001 per cent solution of noradrenaline is administered by intravenous drip in amounts sufficient to maintain blood pressure at 100-110 mm. If the fall in blood pressure does not occur a second tumour is present.

ACTH and Cortisone Therapy

Hans Selye regarded the adaptation mechanism as protective against stress and its action is mediated by the pituitary which in turn stimulates satellite endocrines. The pituitary-adrenal axis has come to be viewed as a stress adaptation safeguard. It is noteworthy that certain types of treatment such as artificial pyrexia, protein shock and insulin shock were employed empirically in conditions now considered to be stress manifestations and these methods probably act by inciting the stress adaptation mechanism.

The adrenal is a complex organ from which more than twenty-five crystalline steroids have been isolated. Selye's thesis has received substantial confirmation from results of investigation with pituitary adrenocorticotrophic hormone which stimulates endogenous production of adrenocorticosteroids.

Until a few years ago the potential range of usefulness of corticotrophin and the corticosteroids was unforeseen and they seemed destined for minor therapeutic rôles as replacement agents in endocrine disorders. Hench and Kendall showed that rheumatoid arthritis and some allied non-endocrine disorders were temporarily suppressed. Early clinical trials were mostly with the collagen diseases and favourable results were noted in rheumatoid arthritis, rheumatic fever, osteoarthritis, disseminated lupus erythematosus and periarteritis nodosa. That the effect was not a group-specific one was proved by the response obtained in other widely dissimilar conditions and it became clear that these hormones could modify many metabolic processes.

The background of Selye's work suggested trial of the hormones in acute emergencies of the alarm variety and the gratifying results in status asthmaticus, acute gout, burns, shock, hæmolytic and hæmorrhagic crises, allergy and drug

intoxications accentuated the importance of the pituitary-adrenal axis as main spring of the body defence mechanism.

The rationale of the hormones is still unknown but it may be said that the action is (unless used as a replacement agent) non-specific and temporary. Tissue reactions towards noxious environment are altered and when used in self-limiting affections they inhibit pathological reactions while morbid activity persists. Thus in diseases the activity of which is terminated by fibrous tissue reaction the baneful effects of fibrosis in the cardiac valves for example may be mitigated or prevented. Pulmonary tuberculosis, peptic ulcer and surgical wound healing may theoretically be adversely affected but it is now clear that in many serious infections like typhoid and miliary tuberculosis the corticosteroids can hold up the tissue reactions and allow effective antibiotic actions to take place. In viral hepatitis and obstinate obstructive jaundice prednisolone and neomycin together have proved beneficial.

In crises such as burns and overwhelming infections where the adrenal cortical function is in eclipse corticotrophin may exert a true replacement effect. That the hormones act at cell level is apparent from results of their application to the eye, nose and synovia.

Adrenocorticotrophic hormone (corticotrophin ACTH)
Extracted from anterior pituitary glands. On injection it stimulates the adrenocortical mechanism, which elaborates in particular the 11-hydroxysteroids. It is inactivated by the gastro-intestinal enzymes and the eosinopenic response is a gauge of its activity. The hormone is usually given intramuscularly but slow intravenous injection shows a much more prolonged effect. The overall effect (in proportional dosage) is much the same as with cortisone provided that the adrenals are able to respond. Cortisone or a related steroid is obviously preferable in some conditions: oral activity is a convenience, and certain undesirable side effects (salt and water retention, vasospasm and hypokalaemia) are less prominent than with ACTH.

Cortisone (11- β -hydro-17-hydroxycorticosterone compound E). Prepared by partial synthesis from bile acids, or more economically from hecogenin (usual). Available as pure

hormone but the micro-crystalline acetate suspension is of equal potency (25 and 50 mg per ml) Where a relatively rapid effect is required e.g. in Addisonian crisis or operative treatment of Cushing's syndrome oral dosage is 50-250 mg daily by divided fractions the upper range being used for rapid control of acute manifestations after which gradual reduction to maintenance level should be effected dosage by intramuscular injection is 100-200 mg daily in six hourly fractions reduced to 40-60 mg according to progress

Hydrocortisone (17 hydroxycorticosterone compound F) Originally obtained by perfusion of an 11-17-corticosteroid (compound S) through the adrenal gland but now prepared synthetically believed to be the naturally circulating form of cortisone The pure hormone and its acetate show marked difference in potency the former being 50 per cent more active than cortisone and the latter much less active than either possibly because of its lower solubility The acetate is used for injection into joints and dermal application A continuous intravenous infusion of hydrocortisone or its hemisuccinate sodium (100-150 mg) may be life saving in acute adrenal failure to bridge the latent period of intramuscular cortisone or oral prednisone

Deltasteroids Prednisone and prednisolone are analogues of cortisone and hydrocortisone respectively They possess similar anti-inflammatory and anti-rheumatic effects but these compounds are five times more active with similar side-effects although the deltasteroids cause less sodium and water retention This latter property makes them preferable in nephrotic and cardio-cirrhotic states and possibly less useful in Addison's disease Peptic ulcer may be reactivated and a history of this condition is usually a contra-indication The fear that surgical incisions will not heal is largely without foundation Dosage is one fifth of cortisone Triamcinolone an α fluoro derivative of prednisolone (Lederkort Lederle Adeortyl Squibb) is reputed more active with less tendency to induce oedema hypertension potassium depletion etc Dosage is on average one third less than that of prednisolone Medrone Upjohn a methyl derivative has similar potency

Prolonged therapy The adrenals may become functionally

inhibited and atrophic with prolonged cortisone or delta cortisone therapy ACTH may cause adrenal hyperplasia and histological signs of regression in the anterior pituitary. There is no evidence that Addison's or Cushing's syndromes have resulted from treatment. This endocrine impairment is reversible after cessation of therapy but in the induced negative adrenal phase the body is asthenic and vulnerable to stresses such as infection and trauma including surgery. Additional hormone dosage will be necessary if such stresses complicate treatment.

Complications. Result from hormonal excess and with careful dosage are usually of minor importance. They are more frequent in women and children than in men.

Changes in fat metabolism increased fat storage. Cushing configuration: moon face and buffalo hump on the back of the neck. The calorie intake should be controlled during treatment.

Changes in carbohydrate metabolism Diabetogenic effect with liberal dosage. If the patient had a normal glucose tolerance previously the condition usually subsides on cessation of therapy. Progressive severity of established diabetes has not been noted. Prevention is by control of carbohydrate intake.

Changes in protein metabolism growth and wound healing. Large doses lead to increased urinary nitrogen excretion and negative balance. Interference with wound healing seems to be of experimental rather than clinical significance. High protein diet, testosterone and potassium have been suggested for prevention of these effects.

Changes in electrolyte balance Sodium and water retention, diminished perspiration loss and increased potassium excretion (more marked with ACTH on account of the increased DCA production under its stimulus). Muscular weakness, low blood pressure and low voltage electrocardiograms are indications of potassium lack. Hypertension may be temporary and due to plethora; a more severe form is caused by adrenergic stimulation and is a contra indication to further therapy. These side effects are dangerous in the presence of myocardial disease or nephritis. For prevention sodium-poor diet and diuretics, potassium by mouth.

Skeletal changes Increased excretion of calcium and phosphate leads to osseous demineralisation and fractures as in Cushing's syndrome. Elderly arthritics are osteoporotic in any case.

Blood changes Disappearance of circulating eosinophils three to four days after commencement of therapy (more marked with ACTH).

Androgenic effects Masculinisation, facial hirsuties, amenorrhoea (women), acne, striae distensae, reduced 17 ketosteroids (both sexes). Dosage should be as low as possible in women and children, especially in brunettes with sallow complexions.

Psychiatric changes Usually euphoria, sometimes insomnia, depression or confusional psychoses. Probably pre-existing mental instability uncovered by treatment which should cease.

The following conditions may show favourable response to corticosteroids

Collagen group

rheumatoid arthritis	polyarteritis nodosa
osteoarthritis (symptomatic improvement)	
rheumatic fever	disseminated lupus erythematosus
sarcoidosis	dermatomyositis
scleroderma	temporal arteritis

Allergic states

bronchial asthma and hay fever	
drug sensitisation	angioneurotic oedema
Loeffler's syndrome	

Blood diseases

haemorrhagic conditions	Henoch Schönlein purpura
acute leukaemia	acquired haemolytic anaemia

Metabolic diseases

acute gout

Endocrine disorders

Addison's disease	Waterhouse-Friderichsen syndrome
Simmonds's disease	Following adrenalectomy for inoperable carcinoma
Adrenocortical hyperplasia	congenital and acquired

Eye diseases (local application of hydrocortisone)

iritis uveitis choroiditis	interstitial keratitis
Stevens Johnson syndrome	sympathetic ophthalmia

Skin diseases

acute dermatitis	pruritus ani et vulvae
exfoliative dermatitis	pemphigus

Various

ulcerative colitis (cortisone orally hydrocortisone locally)	
nephrotic syndrome	emphysema and pulmonary fibrosis
	toxic jaundice

Contra Indications

Cushing's syndrome	hirsuties
diabetes	renal and cardiac disease
hypertension	psychiatric instability

Relative Contra Indications

active or quiescent tuberculo sis	active infections
active or quiescent peptic ulcer	

THE GONADS

Eunuchoidism Results from pre pubertal testicular hypofunction deficiency arising after puberty causes obesity with genital atrophy and loss of libido

Replacement therapy in the form of testosterone is sometimes of considerable value and the propionate is given intramuscularly in dosage of 25 mg for an adult once to three weekly until improvement occurs For maintenance therapy methyl testosterone 50-100 mg daily by mouth or sublingually (5 mg tablets) is worthy of trial Implantation of either preparation in pellet form is a convenient and successful method 300 mg implant corresponds to 4 mg sublingually daily There is no valid basis for the use of androgenic steroids in impotence and the male climacteric Testosterone has been used in combination with chorionic gonadotrophin for cryptorchidism in otherwise normal pubescent subjects Delayed testicular descent in generally undeveloped boys may be treated first with chorionic gonadotrophin e.g. Pregnyl Organon 200-500 i.u.

intramuscularly twice weekly in correct the primary hormonal deficiency later spermatogenesis is stimulated by administration of testosterone 5.25 mg intramuscularly twice or thrice weekly. There is considerable doubt as to the efficacy of this treatment and it is always possible that spontaneous testicular descent will occur at puberty. In boys who are mentally and otherwise physically well developed surgical treatment is preferable especially in view of the hazards associated with inguinal retention.

Ovarian hypofunction. May be primary due to defective ovarian development or secondary to deficient pituitary or thyroid activity. Cases in the first group should have treatment by stilboestrol 1.25 mg daily orally in ten day courses commencing at puberty provided growth is complete prior medication with methylandrostenediol (Protandren Ciba) 25 mg sublingually daily will improve short stature and is less likely than other androgens to induce virilisation. For the secondary group in which general hypoplasia of the genital organs is common serum gonadotrophic hormone and thyroid extract should be given (see p 171). The gonadotrophic hormone e.g. Gestyl (Organon) may be administered in dosage of 1000 i.u. weekly by intramuscular injection.

Ovarian granulosa cell tumours. Cause precocious development with tendency to skeletal overgrowth and the tumour may be large enough to produce abdominal protuberance. Retrogression of the abnormal sexual development follows removal of the tumour.

Metropathia haemorrhagica. Irregular uterine bleeding occurs most frequently in adolescent girls and as a menopausal phenomenon. Before embarking on hormonal therapy a pelvic examination is essential particularly in the menopausal group in order to exclude malignancy. Treatment may be by luteinising hormone or androgens (Gonadyl Chorionic Roussel) 1000 i.u. being given intramuscularly daily until bleeding ceases to prevent recurrence six similar doses may be given on alternate days before the next period. Progesterone is given intramuscularly in 20-40 mg doses daily for four to six days and the series is repeated after an interval of two weeks. Several courses of this order may be

needed. Testosterone antagonises oestria production and encourages the endometrial resting phase. Dosage 100 mg. intramuscularly daily for four doses. Androsalone 25 mg. sublingually for six days at the onset of bleeding is little irritating and therefore preferable. Suppression of the catamenia for several months may follow testosterone therapy but undesirable side-effects such as hirsutism are liable to occur.

Amenorrhoea and oligomenorrhoea. May be due to physical stress, emotion, to constitutional conditions such as malnutrition, anaemia, tuberculosis or to local causes. Oestrogen treatment is successful in cases showing no gross hypoplasia or other developmental defect. Ethinyl oestradiol, a synthetic derivative of oestradiol, is a useful oral preparation (0.05-0.15 mg.) daily in twenty day courses with ten day rest intervals. Serum and chorionic gonadotrophins are also of assistance and may be used in dosage of 1,000 i.u. by muscle on five successive days followed by 300 i.u. for three days. Anaemia should be corrected by dosage with iron.

When evidence of the establishment of a menstrual cycle is forthcoming a synthetic oestrogen should be given daily between the seventh and twenty first days. Progesterone is then substituted (10-25 mg. daily) for four days and withdrawal bleeding may occur three to five days afterwards.

Amenorrhoea. Roussel is a useful combination which contains ethisterone 50 mg. and ethinyl-oestradiol 0.05 mg. (4 tablets) (4 tablets daily on the twenty first to twenty fifth days of the cycle). Several courses are usually required to establish a firm cycle which may subsequently be maintained by oestrogens alone.

Menopause. Unpleasant symptoms such as flushing, palpitation and nervousness are diminished by minimal dosage with oestrogens. Ethinyl oestradiol is well tolerated, and may be taken in dosage of 0.01-0.05 mg. daily for periods of ten to fourteen days. Suitable intake is found by experiment but should stop short of provoking uterine bleeding. Natural oestrone or stilboestrol is more effective against flushing and is given as 0.1 mg. tablets, 4-12 daily until the symptoms are controlled when the patient should revert to diminished intermittent dosage.

Combinations of oestrogens and androgens are sometimes preferable to oestrogens alone as androgens minimise the tendency to breast turgidity and uterine bleeding (Pausan dryl Roussel Mivogen Organon 1-4 tablets daily for ten to twelve days followed by fourteen days rest) Hypothyroidism if present should be corrected Atrophic vaginitis and kraurosis vulvæ are improved by local and general oestrogen therapy

Stein Leventhal syndrome A Cushing like condition in young women characterised by obesity amenorrhœa sterility facial hirsuties and acneiform eruptions associated with fibrotic and polycystic ovaries Hormonal treatment is useless but wedge resection of the ovaries restores menstruation and fertility in most cases

CHAPTER VI

DISEASES OF THE BLOOD

Hypochromic Anemias

From the therapeutic viewpoint this group may be made to include the common microcytic anemia Plummer Vinson syndrome chronic anemia due to hæmorrhage and the hypochromic anemias of infancy and childhood Possible ætiological factors are deficient intake absorption or utilisation of iron and excessive demand in menstrual disorders and pregnancy The presence of contributory factors such as peptic ulcer sepsis tuberculosis and neoplasm must be excluded

In cases where the anemia is mild or moderate (hæmoglobin 60 per cent or over) confinement to bed is unnecessary but strenuous exertion should be avoided If the hæmoglobin is under this figure rest in bed is desirable until substantial improvement in the hæmatological condition occurs

Fresh air and sunlight are valuable therapeutic aids and release from unhealthy working conditions is desirable Dental sepsis or deficiency should be remedied Treatment may be nullified by excessive menstrual loss and gynecological assistance must be sought Hæmorrhoids if bleeding call for hæmostatic measures short of radical operation

A nourishing dietary containing ample protein is essential Iron must be given orally in adequate dosage until the blood picture becomes satisfactory afterwards maintenance therapy for one week in each month may be sufficient The following preparations are suitable for routine use

Ironic Ammonium Citrate Mixture B.P.C. $\frac{1}{2}$ fl. oz. four times daily

Ferrous Gluconate Tablets B.P. 6-12 daily

Lawson's Ferrous Sulphate Tablets B.P. (or as Ferrous Gluconate) 4-8 daily

Enteric coated tablets or capsules are sometimes preferable on account of their freedom from gastric irritation but dysphagic patients swallow liquid preparations more easily. For the occasional patient who is genuinely intolerant of inorganic iron salts a colloidal suspension of the metal may be substituted (Colliron Evans Idoran Coates & Cooper Dose 4-12 drachms daily). Ferrous succinate preparations are well tolerated and utilised e.g. Elixir Ferromyn and Ferromyn Tablets (Calmic). Chelates cause little alimentary upset. Ferroids, Riker (iron aminoates) 3-8 tablets daily Sytron P.D. (sodium ironedate) 8 drachms daily.

Imferon Benger is a stable iron-dextran preparation for intramuscular injection which is very useful for initial treatment of severe or refractory hypochromic anaemia particularly where oral therapy is ill tolerated or the body reserves of iron are depleted. Two ml of the solution (100 mg elemental iron) will raise the haemoglobin level by about 2.5 per cent so that a subject weighing 140 lb with a haemoglobin level of 50 per cent would require (allowing for replenishment of iron stores) 8 daily injections of 5 ml. The daily dose for children is 1.2 ml and for thin or elderly subjects 2 ml.

Constipation is not aggravated by vigorous iron therapy routine purgation should be avoided as it interferes with absorption of the metal. Increase of the fruit and vegetable content of the diet and small doses of liquid paraffin will encourage bowel regularity. Dyspepsia may require temporary alleviation by alkalis and sedatives but in achlorhydric cases the administration of dilute hydrochloric acid with meals may improve digestion.

Convalescence should be lengthy otherwise relapse may occur. A restful holiday in the country or at the seaside is most beneficial. Confirmed iron deficient anaemic females should have regular courses of therapy.

Post haemorrhagic anaemia. Complete rest in bed is necessary with control of the bleeding source if possible. A sedative such as morphine will allay anxiety. If the haemoglobin level falls to 40 per cent blood transfusion should be arranged for. If the blood loss has been sudden the first 3 pints of blood may be given rapidly (fifteen to twenty

minutes) and afterwards a slow drip is used. Full iron dosage (preferably intramuscularly) is instituted as soon as the patient's condition permits. In severe haemorrhage other anti-shock measures must be employed. Moderate warmth should be secured and fluid-electrolyte balance corrected if necessary by intravenous infusion.

Dextran is of limited utility as a blood replacement but is rapidly gaining favour as an anti-shock measure.

The foot of the bed should be raised and in desperate cases binding the limbs tightly will help. Inhalation of oxygen in high concentration is indicated in cases of severe oligæmic shock and it may keep the patient alive until blood transfusion can be set up. Stimulants such as caffeine, nikethamide and pholedrine are rarely of utility. Methylamphetamine hydrochloride in dosage of 30 mg. intravenously will help to maintain blood pressure but it should not be used until the blood volume has been partially restored. Careful record of the general state, pulse rate and blood pressure readings affords the best indication as to adequacy of treatment. Haemoglobin readings do not reflect the true state of affairs during the immediate post-haemorrhagic phase.

Addisonian Anæmia Pernicious Anæmia

The pathogenesis of this disease has not been fully elucidated. The fundamental defect appears to be failure of absorption of vitamin B₁₂ (extrinsic factor) in the upper alimentary tract, due to lack of intrinsic factor present in normal gastric juice. Replacement therapy can be effected by a variety of substances e.g. experimentally by normal gastric contents, fœtal extracts. The first practical therapy was the administration of raw or lightly cooked mammalian liver pulp in amounts of $\frac{1}{2}$ lb. daily (Minot and Murphy). A later refinement was the use of liver extract or desiccated hog's stomach by mouth (Liquid Extract of Liver B.P. 1 oz. daily. Desiccated Stomach $\frac{1}{2}$ 1 oz. daily).

Various combinations of iron, liver, folic acid and vitamins are available commercially but they should not be depended upon for treatment of Addisonian anæmia. Oral preparations are variable in activity and become unpalatable under

prolonged usage they should be used only in exceptional circumstances

The first element of treatment in this disease should be accurate diagnosis. Examination of the peripheral blood and bone marrow must be done before therapy begins otherwise the diagnostic criteria quickly become confused. The expectant treatment of anaemia with buckshot preparations of liver and iron is a real disservice to the patient.

Intramuscular injection of a potent liver extract was until a few years ago the sheet anchor of treatment. Ana-hæmin B D H and Examen Glaxo are two of many excellent preparations which are used in doses of 2 ml daily for the first week. During the second week the liver extract may be injected on alternate days when a satisfactory hæmatological response ensues the intervals are gradually lengthened until a maintenance dosage is arrived at (usually 2-3 ml fortnightly).

Vitamin B₁₂ (cyanocobalamin). Cobalt-containing pigments isolated from liver extracts proved active in remission of pernicious anaemia in amounts as small as 1 µg. It is produced commercially as a by-product of streptomycin manufacture by fermentation of *Streptomyces griseus*. This substance occurs widely in Nature and has been recovered from faeces of normal and pernicious anaemia subjects. Cyanocobalamin is a true vitamin being concerned in growth of animals and probably of children also.

Vitamin B₁₂ has so far proved the most popular effective and economical treatment for Addisonian anaemia although some workers have encountered a tendency for the hæmatological remission to become incomplete within two years. Oral dosage is effective. Distivit Distillers Co. is a cobalamin peptide complex initial dosage 3-10 µg tablets daily for 10 days. Then 1 daily for 1-2 months followed by 10-50 µg daily indefinitely.

Initial dosage is in the region of 50-100 µg by intramuscular injection daily for four or five days after which the frequency may be reduced to twice weekly. In severe cases elderly subjects and those with concomitant infection or neurological complications 1000 µg should be given daily for seven days. When the blood count reaches normal

dosage may be gradually reduced to a basal level of 50-100 μ g fortnightly on this most patients will maintain improvement indefinitely. Subacute combined degeneration of the cord is an indication for trebling or quadrupling the dosage of cobalamun at all stages of therapy.

Folic acid (pteroyl / glutamic acid) Certain members of the vitamin B complex exhibit haemopoietic properties in pernicious anaemia. Of these folic acid, 5-methyluracil, the L-leucyl factor and the citrovorum factor (which is probably folinic acid) are active in macrocytic anaemias. The dose of folic acid is 20 mg daily by mouth and this may subsequently be reduced to 10 mg daily. It should not be used in Addisonian anaemia as it is ineffective for prevention or relief of post-ro-lateral sclerosis. It is however often superior to liver or vitamin B in the macrocytic anaemias associated with sprue, coeliac disease, steatorrhoea and pregnancy.

General management. Includes rest, varied and nourishing diet (containing liberal protein), fresh air and sunshine. If the haemoglobin is under 60 per cent, rest in bed is indicated in order to lessen myocardial strain and hasten recovery. Septic foci should have circumspect treatment but extensive procedures such as dental clearance must be postponed. If the haemoglobin level is under 50 per cent and rapid response is desirable, transfusion of packed cells will produce gratifying improvement in the patient's condition. Oral or intramuscular iron is a useful temporary medication for patients with an initially low blood count and showing rapid response to anti-anemic therapy.

Response to treatment. Judged by improvement in the patient's colour, strength and energy. After a few days anti-anemic treatment the reticulocyte count will rise from a basic figure of about 3 per cent to a critical level of 20-30 per cent which after the tenth day will diminish as the erythrocyte count increases. A steady rise in haemoglobin and erythrocytes should begin after about seven days' treatment. Disappearance of erythroblasts from the peripheral blood, also of the characteristic megaloblastic bone marrow reaction and the reappearance of normal serum bilirubin values indicate satisfactory response. Basal maintenance requirements

vary between individuals and in the same individual over a period regular blood counts should be done to ensure that anti anæmic dosage is adequate

Cheilitis and glossitis Tend to improve under adequate therapy Vitamin B concentrates (particularly nicotinamide and riboflavine) and ascorbic acid may be tried

Diarrhœa Relieved by dilute hydrochloric acid 45 90 minims and glycerin of pepsin 60 minims in water with meals

Subacute combined degeneration and peripheral neuritis The latter responds well and the former improves slowly with massive liver or vitamin B₁₂ therapy Three or four times the usual dosage should be given Unnecessary confinement to bed is avoided The patient should be warmly clad and encouraged to take exercise (in the open air if possible) in order to stimulate the peripheral circulation Massage and re educational exercises improve muscle tone and help the sufferer to regain confidence in his lower limbs

Gastric carcinoma Develops in a significant proportion of pernicious anæmia subjects and should be sought for if unwonted dyspeptic symptoms make their appearance

Other macrocytic anæmias May arise from interruption of hæmopoiesis at various stages Dietetic deficiency anæmia is due to lack of extrinsic factor or protein substrate The tropical macrocytic anæmia described by Lucy Wills is believed to belong to this category These respond to adequate protein intake Marmite or yeast folic acid or liver extract Another variety is caused by surgical interference with the gastrointestinal tract Total gastrectomy and gastroenterostomy may lead to sequelæ of this kind Treatment is as for pernicious anæmia Defective absorption of anti anæmic liver principle may occur in sprue steatorrhœa intestinal obstruction and fistulation Folic acid is effective in cases due to sprue etc. but vitamin B₁₂ is indicated where surgical lesions exist Defective hepatic storage of anti anæmic principle is occasionally encountered in association with a cirrhotic liver and hepatic malfunction may also be operative in macrocytic anæmia of pregnancy Treatment as

for pernicious anaemia. Achrestic anaemia of Wilkinson and Israëls may be due to defective utilisation of anti-anaemic principle by the bone marrow but many are steatorrhoeic. Treatment is not as a rule curative but blood transfusion and folic acid are temporary expedients. Macrocytic anaemia due to bone marrow invasion by tumour cells is little responsive to treatment. For myxoedema anaemias see ■ 154

HÆMOLYTIC ANÆMIAS

These are broadly classified into those due to congenital abnormalities of the erythrocyte and the acquired types due to extra-corporeal causes *e.g.* toxin.

Acholic Jaundice

The characteristics of the congenital type are jaundice, anaemia and splenomegaly. Spherocytosis, increased fragility of the erythrocytes, increased serum bilirubin and urobilin excretion are constantly present. Pigment and calcium gall stones are found in 60 per cent. of cases and leg ulceration is a frequent complication. During a crisis the patient becomes febrile, increasingly icteric, and splenomegalic. Gall-stone colic may be a complication. The acquired type shows similar tendencies but these cases are possibly mild enough to have escaped recognition during childhood. Icterus and increased erythrocyte fragility may be slight, anaemia being the leading feature.

Treatment. A sheltered life is best. Exposure to cold and strenuous exertion should be avoided. Splenectomy is a very effective resource. The gall bladder should be explored, and if stones are present the viscus is removed. Pre- and post-operative blood transfusion is required although overload (with its risk of portal thrombosis) must be prevented. If possible operative treatment should be avoided during a crisis or when the platelet count is high; it is however in severe crises that splenectomy may be life-saving. The post-operative thrombocyte increase may induce venous thrombosis; this should be forestalled by heparin or coumatin therapy at the earliest sign of hæmoconcentration.

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Erythraemia : Polycythæmia Vera

The general routine is that for arterial hypertension and includes a quiet life with limited activity. The diet should be designed to exclude articles rich in iron such as red meats, eggs, liver, thick meaty soups and green vegetables. Considerable symptomatic relief follows venesection (500-1 000 ml) done in under thirty minutes and repeated one to five times yearly to keep the packed cell volume around 55 per cent.

Nitrogen mustards have an inhibitory action on bone marrow. Triethylenemelamine (TEM) 5 mg orally weekly is the most popular cytotoxic agent. Radiotherapy to the long bones and thoracic cage has a slow and somewhat irregular depressant action on the bone marrow.

Radioactive phosphorus induces longer and more satisfactory remissions than the earlier methods of treatment. ^{32}P is best given intravenously in dosage of 2.55 mc. In older patients where the possibility of arterial or venous thromboses arises, one or more venesections should be done (shortly before or after administration of ^{32}P) to reduce the red cell count to near normal. The reticulocyte count will drop to normal about two weeks after an adequate dose and the erythrocyte count should approach normal in six to eight weeks. If no significant fall results a second dose may be given in about three months. Remissions last six to eighteen months although some of three years have been reported.

Erythrocytosis : Secondary Polycythæmia

Causal conditions such as congenital cardiac lesions, pulmonary disease and hæmoconcentration must be taken into account in deciding treatment. Chronic poisoning as by carbon monoxide, phosphorus or arsenic requires appropriate action.

Enterogenous Cyanosis and Methæmoglobinæmia

Parhæmoglobinæmia may be caused by the ingestion of sulphonamides, nitrites, potassium chlorate, acetanilide, phenacetin and phenazone. Constipation with excessive formation of hydrogen sulphide in the bowel may be a factor.

also intestinal infection with the nitrite producing organisms and consumption of well water contaminated by nitrates

Treatment consists of omission of the responsible drug and correction of constipation by liquid paraffin and enemata

Methemoglobinæmia including the familial form can be relieved by intravenous injection of methylene blue (7-10 ml of 1 per cent solution) Ascorbic acid is a more convenient long term therapy 200-400 mg daily orally will control the methemoglobinæmia and cyanosis probably by acting as a substitute for the missing intra-erythrocytic reducing system Chemical reversal of sulphhemoglobin is impossible

Lymphadenoma Hodgkin's Disease

A stimulant régime including good food fresh air sunshine and tonics of iron and arsenic should be exploited For severe anemia blood transfusions are given Radiotherapy is a useful palliative particularly in early cases and those where enlarged lymph nodes threaten to compress important structures e.g. mediastinum and spine In cases of slow development where there is strict localization in peripheral lymph nodes surgical extirpation of the entire regional lymphatic chain may be done as a preliminary to intensive radiotherapy

Alkylamines are the most effective therapy for disseminated lymphadenopathy with severe constitutional disturbance Remissions are sometimes dramatic but not so prolonged as after radiotherapy The nitrogen mustards are effective but triethyl melchloramine (TEM) has the advantage of being active by mouth Several courses of 15 mg over two weeks may be given with intervals of six to eight weeks, as required under strict hematological control Chlorambucil (Leukeran B.W.) is a mustard derivative with few unpleasant side-effects Dose—0.2 mg/kg body weight orally daily for four to six weeks It should not be used within four weeks of substantial radio- or chemotherapy Retrogression of the lymphatic masses and of the splenomegaly occurs, together with improvement in the general condition

Cases of long standing—particularly those with thoracic and abdominal lesions, in whom radiotherapy has been full

exploited—often reach an impasse characterised by anaemia pyrexia and cachexia where they tend to be radio-resistant. If such patients are treated by preliminary transfusions alkylamine therapy may initiate improvement in the general state and restore radio sensitivity.

The Leukaemias

Acute leukaemia may be myeloblastic lymphoblastic or rarely monoblastic. Severe hypochromic anaemia calls for repeated blood transfusion and antibiotics are useful for control of sepsis. Stomatitis and buccal ulcers improve with use of a citric acid mouth wash ($\frac{1}{4}$ 1 fl oz of saturated solution in a tumblerful of water).

6-Mercaptopurine (Purinethol B IV) an antimetabolite of purine bases of nucleic acid exerts an inhibitory action on the blast cells and is useful in acute leukaemia as well as the blastic terminal stages of chronic leukaemia. Average daily dose 2.5 mg/kg body weight orally for six to twenty six months as necessary. Double dosage may be required initially and maintenance may be as low as 1 mg/kg. Regular blood counts must be done. The steroid hormones are useful adjuvants to aminopterin or mercaptopurine: cortisone 100 mg daily or prednisone 25 mg daily.

Chronic leukaemia is commonly myeloid or lymphoid, and may run a course of months or years during which time fair health is possible. Such patients should lead sheltered lives and all possible measures are taken to improve nutrition and resistance. Intercurrent infections must be combated by appropriate antibiotic therapy. Hypochromic anaemia is a constant finding which calls for iron and occasionally for blood transfusion.

Antimetabolite drugs are of little value when the cells are dividing slowly as in the chronic leukaemias. Drugs which act as cell poisons are more effective particularly in the myeloid variety.

Urethane (ethylcarbamate) by mouth in dosage of 3.5 G daily to a total of 80-170 G has been tried in leukaemia and myelomatosis. This drug is more effective in chronic myeloid than in lymphatic leukaemia and in favourable cases it will produce temporary correction of the blood picture similar

to that obtained by radiotherapy. Nausea with gastric disturbance is an objection, but this may be avoided by use of the rectal route.

The nitrogen mustards have a variable and often disappointing effect in chronic leukaemia. Mustine hydrochloride (2,2-dichlorodiethylmethylamine) is given by slow daily or alternate daily intravenous injection of 5 mg. (or less according to body weight) for six doses. If necessary this course may be repeated after 4 to 6 weeks.

Karnofsky introduced triethylenemelamine (triellamine TEM) as a treatment of the Hodgkin's-leukaemia group. Its action is similar to that of the nitrogen mustards, but it can be given orally in enteric-coated tablets. Dosage is 2.5-10 mg. daily one hour before breakfast for two doses. This routine is repeated after a week, provided that the white cell count is satisfactory. The maximum effect is noted in two to three weeks, and further treatment is decided by the patient's blood count and general condition. Side effects are nausea and vomiting. Busulphan (Myeleran B.V.) is effective only in chronic myeloid leukaemias. The dose is 4-6 mg. orally daily for as long as improvement is shown, usually four to sixteen weeks. As the granulocyte count falls the dose is reduced and omitted when the level of 15,000 is reached. This substance may be tried in cases judged unsuitable for radiotherapy, and in those who have become radio-resistant.

Radiotherapy. X-ray treatment remains the most generally applicable and efficacious measure. It will often defer invalidism and prolong life. A series of treatments to the splenic area, bones and affected lymph nodes will produce a satisfactory fall in the leucocyte count, diminution in spleen size and a tendency to normalisation of the differential white cell distribution. Dose 4-9 mc. orally according to cell count and more important still the clinical state appears to have no advantage beyond a saving of time in treatment and lessened liability to radiation sickness.

Chronic lymphocytic leukaemia when active responds best to TEM or chlorambucil, although mustine is occasionally more effective in alternate daily intravenous dosage of 5 mg. (or less according to body weight) for six doses. If necessary this course may be repeated after six to ten weeks.

Irradiation of the spleen and gland masses and ^{32}P are occasionally useful in alternation with cytotoxic therapy while cortisone and related steroids are useful adjuncts

Agranulocytosis Neutropenia

The characteristic features of these conditions are serious reduction or absence of polymorphonuclear leucocytes from the blood and absence of myeloid reaction. Fever, anaemia and ulcerative or gangrenous lesions of the mouth and pharynx are common concomitants. A similar syndrome may terminate leukaemia and myelophthisic anaemias. Agranulocytic angina may occur without obvious cause or follow the administration of certain drugs such as barbiturates, amidopyrine, chloramphenicol, trovudone, PAS, phenylbutazone, sulphonamides, organic arsenicals, gold and thiouracil. The mechanism of sensitisation is not understood but is probably of the nature of an anti-white cell agglutinin.

Treatment consists in withdrawal of the offending drug if still in use. Cure usually follows in seven to twenty-eight days. Rest in bed is necessary until a satisfactory marrow reaction occurs. Liberal diet, fresh air, iron and vitamin concentrates especially of B and C are useful. Oral sepsis usually responds to citric acid, mouth washes and antibiotics. Septicaemia accounts for most fatalities in neutropenia and appropriate antibiotics in heavy dosage are the most important item of treatment. Penicillin should be given (2.5 mega units daily) until recovery is complete or until laboratory data suggest substitution of a more effective antibiotic. BAL should be used in cases presumably due to poisoning by arsenic, gold or mercury (1.5 ml of 10 per cent oily solution deeply intramuscularly four hourly for two days then twice daily for six days). Blood transfusion is a useful standby in the presence of anaemia and fresh blood should be used if thrombocytopenia and haemorrhagic features are present (the leucocyte replacement factor is negligible). Pentose nucleotide, members of the vitamin B series, iron, folic acid and liver extracts are valueless. Cortisone and related steroids in large doses are useful in accelerating clearance of the offending antibody.

HÆMORRHAGIC STATES

Purpura

There are three main groups—those showing deficiency of essential factors such as prothrombin those showing platelet deficiency and those with increased capillary permeability

Infections e.g. meningococcal give rise to purpuric eruptions and the drug group includes arsenicals gold sulphonamides phenobarbitone and coumarins. Other causal factors are allergic states exposure to x radiation vitamin C deprivation renal hepatic and blood diseases malignancy and senility. Idiopathic cases have a chronic course with remissions which tend to become more prolonged after adult life is reached. The purpuric trait although dormant may be reactivated by pregnancy stress etc.

Purpuric rashes rarely require treatment but hæmorrhage from mucous surfaces may be troublesome. If accessible clots should be removed and pressure dressings soaked in fresh 1 : 10 000 solution of Russell's viper venom (Stypven B.W.) applied. Control of infection in bleeding sites or hæmatomata by suitable antibiotics and replenishment of depleted iron stores are necessary. For extensive purpuric affection rest in bed and transfusion of freshly drawn whole blood is indicated. Steroid hormones should be given to tide the patient over an acute hæmorrhagic crisis (cortisone 25-50 mg six hourly orally hydrocortisone 100 mg by vein twelve hourly reducing the dosage as soon as feasible). Splenectomy is of value for resistant cases.

Idiopathic thrombocytopenic purpura is characterised by diminution in the platelet count, prolonged bleeding time and positive capillary resistance tests. Immediate benefit often follows splenectomy but the operation should if possible be postponed to a quiescent interval. Transfusion (fresh blood) is usually necessary before and after surgical intervention. Re-establishment of a normal thrombocyte count may be expected within seven to ten days of operation.

ACTH cortisone and dexamsteroids have been shown to stimulate thrombocyte production in some cases of Werthof's disease and these hormones increase capillary

resistance thus lessening the hæmorrhagic tendency in all purpuric states. By their use in conjunction with blood transfusion desperately ill children may be conditioned sufficiently to undergo splenectomy.

Hæmophilia

The patient should beware of trauma and surgical manœuvres are to be discouraged unless essential and undertaken in hospital. Intramuscular and subcutaneous injections are best avoided. Blood transfusion is required in hæmophilic crises for restoration of antihæmophilic factor. Freshly drawn blood is desirable but in emergency stored blood or plasma (preferably fresh) will serve. After the first sizeable transfusion small amounts (50-100 ml) of blood or plasma at four or six hourly intervals are sufficient to keep the coagulation time at under fifteen minutes thus averting further hæmorrhage if severe bleeding has led to anæmia full replacement with fresh blood is necessary. Antihæmophilic globulin is likewise temporarily effective. Unfortunately patients who have had frequent treatment courses tend to become refractory to blood plasma and antihæmophilic globulin. Anti hæmophilic globulin of animal origin may be used to cover emergencies like abdominal operations but this measure is not repeatable.

Effusions of blood into the connective tissues should be left alone. Joint aspiration may be necessary to preserve joint function and should be done with strict asepsis after adequate replacement of AHG. Hæmarthrosis is met by immobilisation and bandaging. Orthopædic treatment may be desirable later. Local hæmostasis is secured by the application of pressure dressings soaked in thrombin solution. Fibrin foam is also effective.

Routine dental care is essential and caries should be arrested as promptly as possible. Extraction becomes imperative sooner or later and should be done in hospital with preliminary transfusion.

CHAPTER XII

DISEASES OF THE KIDNEYS

Acute Glomerulonephritis

Rest in bed is essential and should be prolonged until urinary output and concentrating power are regained. As a rule four to six weeks rest is sufficient and if recovery be delayed beyond this period the probability of chronic renal damage arises. Hematuria usually clears up quickly albuminuria and cylindruria are more persistent but bed rest need not be indefinitely prolonged on account of their presence. The patient must be protected from chill and draught and a long sleeved woollen bed jacket provided there is then no necessity to nurse him between blankets.

With regard to diet the initial allowance should be 1½ pints of sweetened fruit drink daily with bread, biscuits honey and preserves after a week one pint of milk may be added. During the stage of oliguria excessive fluid intake does no good but encourages oedema. When renal permeability returns nothing is gained by starving the patient of food or fluid. The increase in fluid allowable is proportionate to the improvement in renal output but if oedema is pronounced these figures should be made to correspond. Later the diet may be enlarged to include porridge cereals bread toast and biscuits butter jam and honey milk puddings jellies vegetables and fruit. Adequate vitamin intake should be ensured from the outset. Improvement in the renal condition as evidenced by disappearance of casts and blood from the urine restoration of normal blood urea level and satisfactory renal concentration tests is an indication for addition of protein to the diet notwithstanding the presence of albuminuria. One helping of egg meat or fish may be given daily and increased according to progress. Salt is best omitted and highly cellular foods such as butchers' offals are undesirable.

The urine should be kept alkaline to litmus by fruit juices, citrates and bicarbonates provided that oliguria and potassium retention are absent.

Iron deficiency anemia is common in nephritis and will retard recovery unless actively treated. Purgatives and diaphoretics should be withheld as they merely increase the patient's discomfort. Daily bowel action may be secured by the use of magnesia and liquid paraffin.

Convalescence should be tardy and physical activities regained slowly. The patient should be warned against chills, damp clothing and footwear and he must guard as far as possible against infections of the upper respiratory tract. Septic foci are dealt with during a quiescent phase and surgical interference can often be made less provocative of nephritic activity by the use of penicillin or other antibiotic.

Edema may be a distressing complication of acute nephritis. A water balance chart should be kept and the intake adjusted to correspond with output until diuresis appears. Persistent oliguria should be met by institution of the dietetic measures described under Anuria. Attempts at initiating diuresis by hypertonic venoclysis are dangerous and ineffectual. Convulsions may occur particularly in children and are due to cerebral edema and angiospasm. Lumbar puncture with removal of 10-30 ml of cerebrospinal fluid is a useful procedure. If unsuccessful recourse must be made to venesection (10-20 oz.) followed by a dose of pentobarbitone by vein. Oral sedation may be desirable for a day or two until the convulsive tendency has waned. Hypertonic solutions are justifiable only in resistant cases. 25-100 ml of 10 per cent glucose by vein is least harmful.

Congestive cardiac failure may make a sudden appearance and is productive of severe discomfort. The best treatment is morphine gr $\frac{1}{4}$ intravenously, venesection and oxygen inhalation. Digitalis is rarely of assistance.

Acute Hemorrhagic Nephritis

Common in childhood and frequently follows acute infections. The condition is not clearly demarcated from acute glomerulonephritis but is usually benign and carries a good

prognosis although this cannot be guaranteed in any given case. Massive but transient hematuria with albuminuria and cylindruria are common features. Hypertension with cerebral symptoms occurs in a proportion of cases. Treatment is on the lines indicated for acute glomerulonephritis.

Subacute and Chronic Glomerulonephritis Nephrotic Types

May follow an attack of acute nephritis although in some instances no such incident can be identified. There is great variation in the clinical findings within this group but heavy albuminuria with blood and casts in the urine is common and hypochromic anemia is usually a feature. There is a tendency to salt retention, this with protein loss in the urine and anemia encourages the onset of oedema. Nitrogen excretion is usually normal.

These patients do better in a mild equable climate. A quiet regular life should be enjoined and suitable outdoor exercise allowed during element weather. Strenuous physical exertion, exposure to damp and cold and indulgence in alcohol are harmful. Coincident infections should be treated and reasonable precautions advised against respiratory and intestinal infections.

A diet rich in protein is beneficial by this means the urinary output is increased and the loss of protein compensated for. 120-150 G daily is a fair allowance but is subject to adjustment in accordance with appetite. If there is evidence of lipid retention the fat content should be low but carbohydrate may be liberal.

If oedema is present rest in bed and a low sodium diet should be ordered (less than 0.5 G daily) which will usually be more effective in controlling oedema than fluid restriction. For patients showing haemoglobin deficiency iron is a valuable remedy. Careful watch must be kept on the electrolyte balance as these patients readily acquire a sodium-potassium lack.

Diuretics are sometimes of service in nephrotic cases and urea is traditional but nauseating. dose gr 100-200 daily in orange juice and water. The mercurial diuretics are often satisfactory if nitrogen retention is absent, but their irritant

effect on the already damaged kidney structure precludes their use in some cases. Mersalyl 1-2 ml may be given intramuscularly at intervals of four days after the effect of a preliminary dose of 0.5 ml has been observed. A better response may be obtained from two injections at an interval of twenty-four hours followed by a week's rest. Ammonium chloride gr. 10-20 should be given four times daily by mouth so as to overlap the period of mersalyl administration. Oral diuretics are effective and much less toxic than mercurials. They may be used to implement the latter and in cases no longer responsive to mersalyl in moderate anasarca they are often sufficient alone. Chlorothiazide (Salutic, Merck Sharp & Dohme) causes marked increase in the renal output of chloride and sodium. The usual dose is 2-4 or 5 G tablets on four consecutive days weekly. Chlorothiazide is practically non-toxic and 10 tablets may be given on the first day. Potassium loss may be considerable and supplements may be necessary. Amisometradine (Reliston, Searle) also increases sodium excretion and chloride in equimolecular amounts. Dose 0.4 G tablets 4 on the first day and 2 daily thereafter. Cation exchange resins have been used orally and rectally to control oedema by increasing sodium elimination by the bowel. Their effect is variable but they are helpful in some cases. Acute infections should receive energetic treatment.

Blood transfusion will provide a valuable stimulus to recuperation in anæmic and dropsical subjects and concentrated plasma (two to five fold) may be used as a means of restoring the serum osmotic tension and inducing diuresis. Intravenous dextran infusions have also been tried. Their use appears to be free from untoward reaction but unfortunately the effect is as ephemeral as that of blood and plasma.

Purgatives should not be given as a routine. Magnesium hydroxide, sulphate or cascara are safe for occasional use. Effusions into serous cavities should be aspirated but mechanical drainage of the lower limbs avoided if possible.

Cortisone and ACTH cause fluid retention followed by a withdrawal diuresis. ACTH (15-60 mg six hourly intramuscularly for twelve days and repeated as necessary) has

given better results than the corticosteroids, although the recently introduced methylprednisolone may prove of value in nephrosis. In nephrotic children temporary improvement has followed therapeutic malaria, thyroid and nitrogen mustard, but these methods do not appear to have any scientific basis.

Chronic Glomerulonephritis with Vascular Degeneration

There is no rigid demarcation of this group from the one considered above, and intermediate stages are frequently found. Typically water and salt retention are absent, but azotemia with cardiovascular degeneration and hypertension are common. Progressive failure of renal function is inevitable, and treatment is purely symptomatic. Moderate restriction of protein intake is theoretically desirable, but starvation diets merely add to the patient's misery. Normal carbohydrate intake may be allowed. In view of the tendency to acidosis which arises in the later stages, the acid ash value of meat and starch should be compensated by increasing the fruit and vegetable allowance, and by citrates.

Uremia. A frequent termination of chronic nephritis, and in these circumstances treatment is wholly disappointing. Diet should be reduced to semisolids and liquids, and liberal fluid intake by mouth is desirable. Alkali in the form of sodium bicarbonate is given in doses of 2 drachms hourly until the urine becomes alkaline, in order to combat acidosis. Nausea, hiccough, vomiting and diarrhoea are serious and intractable symptoms, and indications for intravenous administration of 4 G. of sodium bicarbonate in 500 ml. of physiological saline or 10-20 per cent glucose. In chronic uremia intravenous fluids must be used with caution on account of the risk of pulmonary edema. Chlorpromazine (Largactil, Eli & B.) 25 mg. by vein or muscle is good symptomatic treatment.

Headache, restlessness and convulsions are due to electrolyte imbalance, and the case should be investigated along these lines. Acidosis if present should be corrected. Hyperkalemia commonly complicates renal failure. Venesection (10-20 oz.) and withdrawal of cerebrospinal fluid by lumbar puncture may be tried. If the convulsions are not arrested by

these measures recourse may be had to intravenous injection of hypertonic glucose solution. Hypocalcaemia is present in some cases of chronic nephritic uraemia here the sedative effect of calcium salts by the intravenous route may be exploited. Insomnia is often troublesome and calls for the use of hypnotics. Phenobarbitone should be tried in the first instance but morphine may be necessary later.

Myocardial failure is met by digitalis, morphine and inhalations of oxygen. Renal asthma is compounded of acidosis and circulatory failure. Alkalinisation, morphine and oxygen inhalations give some relief.

Extrarenal uraemia. Occurs in conditions of alkalosis e.g. persistent vomiting and overdosage with alkalis. Urea retention with increased blood alkali reserve and the passage of dilute alkaline urine are characteristic (In renal uraemia acidosis is the rule.) Alkaline medication should be stopped and 10 ml. of 10 per cent calcium gluconate given intravenously followed by normal saline (see p. 205). In cases of vomiting due to pyloric or high intestinal obstruction the possibilities of surgical relief must be explored.

Anuria. The obstructive type may complicate renal calculus. Until the renal block has been overcome fluids should be limited to the amount necessary to relieve thirst (maximum 1 litre daily). Catheterisation of the ureter or renal pelvis may relieve calculous anuria. If unsuccessful nephrostomy will be necessary.

Anuria due to tubular necrosis may follow renal circulatory failure or poisoning as in shock states, ischaemic muscle necrosis, incompatible transfusion reactions, mercurial and sulphonamide intoxication. The prognosis of this serious state has been considerably improved by introduction of dietetic and artificial kidney methods. By means of a high calorie non protein diet nitrogenous retention is kept at a minimum by exclusion of salts and reduction of fluid intake to that sufficient to balance extrarenal fluid loss. Rest to the damaged kidneys is assured.

In mild cases the patient should be fed on a lactose and water diet until evidence of renal recovery is forthcoming. Patients more severely ill may be treated by a Bull régime or more simply by a diet of 700 ml. of 50 per cent glucose daily.

through an indwelling Ryle's gastric tube. But if excessive vomiting, diarrhoea or intestinal ileus presents, the intra-gastric tube must be abandoned in favour of a caval one. J. W. Chambers and George South (1957) use a No. 9 F cardiac catheter inserted through the right great saphenous and right femoral veins, the tip lying in the inferior vena cava just above the renal veins, where rapid dilution of the infusion fluid (50 per cent. glucose plus any necessary electrolyte replacement) is assured. 1,000 units of heparin is added to each 500 ml. of infusion fluid, and the drip maintained continuously until renal function returns.

After an anuric period of eight to fifteen days the reformed tubular epithelium regains its diuretic function. During the stage of free diuresis the tubular absorption mechanism is still defective, and a similar state of affairs may arise also in chronic nephritis (Thorn's salt losing nephritis). Electrolyte depletion, especially of sodium and potassium, may produce a clinical picture akin to that of Addisonian crisis. Electrolyte deficiency should therefore be replaced quantitatively. Throughout, anaemia must be corrected by infusion of packed cells and infection combated by appropriate antibiotics (in small doses during the anuric stage).

Peritoneal and intestinal dialysis techniques are effective but require the presence of experienced personnel. Artificial kidney methods postulate elaborate apparatus as well. Intestinal dialysis will reduce the serum potassium level which tends to be dangerously high in prolonged anuria.

Resonium A orally or rectally is also effective and less troublesome.

INFECTIONS OF THE URINARY TRACT

Acute Cystitis

This is the most common manifestation of urinary infection. General treatment consists of rest in bed, warmth, light diet and administration of sufficient sedative to prevent loss of sleep from urinary frequency and irritation. An easy daily bowel evacuation should be secured, but harsh purgatives aggravate the urinary symptoms. Before embarking on

treatment a catheter specimen of urine or in males a mid stream specimen should be examined bacteriologically as a precise diagnosis is essential. Liberal dosage with Potassium Citrate and Hyoscyamus Mixture **|| P C** is excellent initial therapy.

Sulphonamides These drugs give brilliant results in uncomplicated infections by sensitive organisms. The soluble sulphonamides are active against *Esch coli* and its variants, hemolytic streptococci and some strains of staphylococci and enterococci. Trisulphonamide Tablets **|| N F** are popular for urinary antiseptics and preparations of the Lederkyn type (12 tablets daily) are good in elderly patients. As sulphonamides are concentrated in the urine during excretion large doses are unnecessary provided that the fluid intake be kept within reason.

Kidneys damaged by nephritis excrete sulphonamides slowly and effective urinary concentrations are difficult to attain; cautious dosage is essential in such cases. Their bacteriostatic action is maximal in alkaline urine and citrates or bicarbonates should be given concurrently. An adult should receive 2 trisulphonamide tablets six hourly for four days and then thrice daily for four days. For a child of six years 2 G and for an infant 1 G daily is adequate dosage. Some cases relapse shortly after completion of such a course and for this reason it is often desirable to continue with the sulphonamide for a further three or four days using half dosage.

A clearance test should be taken a few days after treatment has ceased. The urine should be free from albumin and pus and sterile on culture.

Penicillin Is effective in urinary infections caused by hemolytic streptococci, coagulase positive staphylococci and diphtheroids. Urinary reaction does not affect its efficacy. Dosage varies according to the pathological lesion: a simple pyelitis will respond to 1 mega unit daily by muscle but cases of pyelonephritis and renal carbuncle should have double or treble dosage.

Streptomycin Has an inhibitory action on the five most common Gram negative urinary invaders. *Esch coli* infections are equally well controlled by sulphonamides but

streptomycin may be used as an introductory or follow up course in cases of long standing and in mixed infections — *E. coli* and enterococci. The urine should be kept alkaline. The dose is 1.2 G daily for four days by intramuscular injection. Unfortunately streptomycin resistance develops very rapidly in urinary pathogens so that this drug has only occasional indications.

Tetracyclines and chloramphenicol Active against a wide range of urinary invaders and resistance is not an important factor. The tetracyclines are valuable for haemolytic staphylococcal and streptococcal infections whereas chloramphenicol would be preferred in infections with bowel organisms. Polymyxin is the antibiotic of choice in *Pseudomonas* infections or a combination of oxytetracycline and streptomycin. streptomycin and chloramphenicol is another effective combination for infections resistant to straightforward chemotherapy. Erythromycin is stated to be most effective in *Streptococcus* infections. Nitrofurantoin (Furadantin, Duncan, Flockhart) is active against most common urinary invaders and successes have been reported in *Proteus*, *Aerobacter* and some *Pseudomonas* strains. Dose 50-100 mg. orally four times daily.

The advent of efficient urinary bacteriostatics has not lessened the need for adequate surgical drainage but surgical interference has been rendered safer by their use. An element of urinary stagnation is usually present in refractory or relapsing cases although reinfection occasionally occurs from an extra urinary focus such as the teeth, gall-bladder or bowel. Prostatic obstruction, renal calculus and developmental anomalies demand appropriate surgical treatment, otherwise medical measures are doomed to failure. Relapsing urinary infection with bacterial invaders should call to mind the possibility of tuberculosis being present as well.

Pyelitis of pregnancy is sometimes obstinate on account of the element of ureteric obstruction present. Sulphonamides are well tolerated. Cases showing signs of ureteric obstruction such as severe renal pain, rigor, vomiting and fever should be nursed in the prone or left lateral position with the foot of the bed raised.

Abacterial pyuria is an uncommon condition but it is disturbing because of the presumption raised that the case may be one of tuberculosis. It has been regarded as a virus disease possibly associated with Reiter's syndrome. The condition is self limiting and there is no effective therapy.

Renal Tuberculosis

Found in association with tuberculosis elsewhere and the general treatment appropriate to that infection is applicable. Streptomycin and the adjuvant drugs *p* amino salicylic acid, isoniazid and thiosemicarbazone are of value in all but chronic fibrocaseous lesions of the kidneys and bladder here the foci are avascular and uninfluenced by drugs. Fibrosis of the ureters and bladder may even be aggravated by their use.

Combined courses of streptomycin and the auxiliary medicaments in turn will clear the urine of *Mycobacterium tuberculosis* in the early stages where radiology shows no definite involvement of the kidneys. For more extensive infections a combination of streptomycin 1 G intramuscularly every third day, PAS 15 G daily and isoniazid 300 mg daily for six to twelve months after the urine has cleared and symptoms disappeared is desirable.

Surgical treatment may be necessary to remove a small quiescent polar focus where disorganisation of one kidney or bilateral involvement exists. The major focus should be removed by nephrectomy.

Renal Calculus

A patient who is passing renal sand or small concretions should be instructed to increase his fluid intake to 5 or 6 pints daily. Patients immobilised for long periods should by some means have their position altered frequently to avoid recumbency stones which are usually apatite (calcium phosphate). In practically all other cases of calculus the urine is acid i.e. oxalate or uric acid stone and must be kept neutral or just alkaline to litmus by administration of Potassium Citrate and Hyoscyamus Mixture B.P.C. Excessive alkalinity leads to phosphatic incrustation of the

existing stone in which case urinary acidifiers such as acid sodium phosphate or ammonium chloride must be substituted. Uric acid deposition is met by exclusion of purine rich foods like liver kidneys and sweetbreads and maintaining the urine alkaline. The consumption of green vegetables should be encouraged. Oxaluria is an indication for omission of rhubarb spinach tomatoes strawberries asparagus beetroot potatoes and chocolate.

Acid and alkaline ash diets are occasionally used for prevention of recurrent stone. The low phosphorus acid ash diet with urinary acidifiers may be tried in cases of calcium phosphate disposition although its use may cause mobilization of calcium from bony structures and subsequent deposition in the urinary tract. It consists of cereals bread pastry potatoes sugar peas beans beetroot and mushrooms unsalted meat fish eggs and unsalted butter. Milk fruit and vegetables (except those mentioned above) are omitted. The urinary pH should be maintained at 5.4 (rose pink to methyl red). Aluminium carbonate or hydroxide orally encourages fecal diversion of phosphate.

The alkaline ash diet with citrates is used for uric acid or urate disposition, and consists of milk butter cheese fruits and vegetables. For oxalate calculi the diet should exclude chocolate and fruits and vegetables of high oxalate content. Calcium intake should be low (under 1.5 G daily). Nothing is gained by altering urinary reaction.

Hyperparathyroidism should be thought of in multiple or recurrent stone formers particularly with apatite or oxalate stones.

Frien recommends continuous salicylate medication for prevention of recurrence in predisposed subjects.

Many small renal stones are passed spontaneously. Stones which give a radiological opacity less than $\frac{1}{2}$ inch in diameter should have their progress checked regularly by x rays. Calculi which by reason of size or position cannot be passed spontaneously should be removed by operation provided that the patient's condition is good. If the urine is infected, a preliminary chemotherapeutic course should be provided. In view of the liability to further calculus formation a post-operative regime on the lines discussed above is

advisable a large urinary output is the most important factor in prevention

The surgical repertoire in nephrolithiasis is extensive. For a stone which is moving radiological observation and if below the pelvic brim and under 1 cm diameter cystoscopic dilatation of the distal ureter may permit extraction of the stone; if not uretero-lithotomy must be done. An imprisoned renal calculus may be delivered by pelvic or parenchymal approach. Partial nephrectomy may be desirable in the event of an irreversibly dilated polar calyx. A staghorn stone should be fragmented and extracted but if the kidney is hopelessly damaged nephrectomy is indicated. Bilateral staghorns present a very delicate problem where the scope of the surgical project must depend on renal function.

Renal Colic

First essentials are rest in bed and warmth to the painful flank. Immersion in a hot bath is sometimes helpful. Morphine gr $\frac{1}{2}$ with atropine gr $\frac{1}{100}$ should be injected; the former intravenously if necessary. Pethidine 50-100 mg and methadone 10-20 mg intramuscularly or intravenously are also effective. Calcium chloride (20 ml of 5 per cent solution intravenously) has been recommended in obstinate cases but some yield only to chloroform inhalation. Lumbar sympathetic block affords relief for severe and protracted colic.

Further treatment is that of renal calculus.

FLUID BALANCE WATER AND ELECTROLYTE DEPLETION

Water forms about 60 per cent of the human body weight. It may be considered as in two main compartments: (a) the extracellular compartment representing 20 per cent of body weight and containing blood plasma (5 per cent of body weight) and interstitial fluid including lymph (15 per cent of body weight); (b) the intracellular compartment (40 per cent of body weight).

The cell membranes are permeable to water which moves from one compartment to the other the motivating force being various equilibrium reactions e.g. pH osmotic pressure as a general rule tonicity takes precedence over volume. Water intake is by way of swallowed liquid (1,200 ml) 1,000 ml from solid food and 300 ml from oxidation processes (preformed water from disintegration of body tissues). The main physiological losses are 1,500 ml as urine and 600 ml each by skin and lung. Selective renal filtration, mediated by hormones (mostly pituitary antidiuretic and adrenocortical) keeps the amount of retained water optimal assuming intact renal function. The kidney excretes or conserves by reabsorption from the glomerular filtrate essential substances like water sodium chloride and glucose. This stabilisation function is less precise in infants because the ability of the kidney to concentrate urine is limited. Perspiration loss and metabolic rate are higher so that fluid imbalance can occur rapidly and in serious form.

Another important factor in fluid regulation is the continuous interchange of water and electrolytes which takes place in the intestinal tract. If intestinal fluid is lost by vomiting diarrhoea continuous aspiration or fistulation, dehydration and electrolyte imbalance surely follow.

The *extracellular fluid* contains a variety of ionic and non ionic substances but sodium chloride ions are of most importance in the present connection. For electro-neutrality the sum of the basic ions must equal the sum of the acidic ions and the use of the milliequivalents per litre convention instead of milligramm-% per 100 ml gives a graphic representation of the respective combining powers of electrolytes in body fluids. For example plasma contains 155 milliequivalents per litre each of anions and cations. Conversion is simple

Equivalent weight = weight of atom or molecule divided by valency

$$\text{mEq/litre} = \text{mg/100 ml} \times \frac{\text{10 valence}}{\text{atomic weight}}$$

$$\text{mg/100 ml} = \text{mEq/litre} \times \frac{\text{atomic weight}}{\text{10 valence}}$$

<i>Ion and valence</i>	<i>Atomic weight</i>
Na ⁺	22.997
K ⁺	39.098
Ca ⁺⁺	40.08
Mg ⁺⁺	24.32
Cl ⁻	35.457
HCO ₃	61.018
H ₂ PO ₄	96.996
HPO ₄	95.989
SO ₄ ⁻	96.066

By means of various buffer mechanisms the kidney is enabled to get rid of acid and alkali increments without alteration of pH or damage to the tissues. Metabolic disturbances which affect acid base balance often cause abnormal water and salt loss also.

The *intracellular fluid* is more complex in constitution than the extracellular and it is more difficult to fathom its changes. Potassium is the main cation, magnesium being next in amount. The anions are phosphate, sulphate and protein. Cell membranes are not readily permeable to sodium and potassium, nor do magnesium and phosphate by intravenous injection enter the cells freely; this makes absolute measurement not truly indicative of the patient's electrolyte balance at any given time and influencing the intracellular fluid composition may be difficult and dangerous. Alteration in one compartment induces compensatory changes in the other. In the case of sodium depletion the serum sodium reflects only partially the extent of the loss, as water from the extracellular compartment passes into the cells to maintain osmoticity. Another difficulty is that according to the view of Peters, cells may store base in an osmotically inactive form, e.g. large molecule storage as in the case of glucose glycogen. Potassium and phosphate can perhaps be similarly tucked away intracellularly.

Marriott has emphasised the distinction between water depletion and sodium deficiency. The former usually follows failure of intake; thirst is a constant symptom, followed by dry mouth, oliguria, the urine being of high specific gravity and normal chloride content. Loss of weight, increased

serum sodium and decreased potassium follow. The volume of fluid in the extracellular compartment is maintained by transfer from the intracellular space unless water depletion is severe. This syndrome is reversible by giving water but water deprivation plus muscular exertion and hyperpnea in a hot atmosphere can be rapidly fatal. For water depletion in a conscious patient give 1.3 litres if unconscious give 2 litres of 5 per cent glucose solution or tap water by rectal drip. In the post-operative state or if there is renal damage give only enough to relieve thirst.

McCance induced pure salt depletion in human subjects. A few days after a definite sodium deficit was incurred as shown by a fall in serum and urinary sodium with tendency to raised blood urea a syndrome appeared suggestive of Addison's disease (apathy lassitude anorexia nausea and vomiting muscular cramps). No diuresis resulted after water ingestion but the symptoms were aggravated. Lowering of blood pressure with decreased cardiac output increased blood viscosity and peripheral circulatory resistance followed.

Combined salt and water depletion frequently exists usually in consequence of abnormal renal or extrarenal activity. In uncontrolled diabetic states glucose excretion by the kidney implies coincidental loss of salt. In salt losing nephritis and lower nephron nephroses reabsorption of salt may be markedly reduced. An uncorrected extrarenal loss of salt and water as in diarrhoea or continuous gastric suction gives rise to a combined depletion of the extracellular fluid which is partially compensated from intracellular fluid. Symptoms are a combination of those enumerated above—apathy thirst nausea oliguria with peripheral vascular collapse. A sodium deficit may exist with normal or raised serum sodium values on account of water loss by the kidney.

The position may be further complicated by an abnormal acid base balance as chlorides form an important part of the buffer mechanism. Estimation of urinary chlorides as by Tannus's test is misleading as in diabetic acidosis the presence of buffer chlorides in the urine may mask a plasma chloride deficiency. Conversely patients with high plasma chloride levels may at times fail to excrete chlorides.

Normal values

Plasma sodium	137-147 mEq /litre
Plasma chloride	100-105 mEq /litre
Plasma bicarbonate	$\frac{25-30}{125-135}$ mEq /litre

If the sum of chloride and bicarbonate values lies outside the range of 125-135 mEq /litre a sodium abnormality can be inferred. In the average patient a deficit of 10 mEq /litre in plasma sodium means a total body deficit of 500 mEq or about 30 G of sodium chloride: this should be replaced as 300 ml of 10 per cent sodium chloride intravenously over three hours. The plasma bicarbonate figure gives information regarding the acid-base position: being low in acidosis and high in alkalosis: the opposite applies when these arise from respiratory causes. Black's rule for correction of salt deficit is

$$\frac{140 - \text{plasma sodium in mEq /litre}}{3} = \text{litres of N/1 NaCl required}$$

Potassium salts should also be given during correction of severe sodium deficit as the lack is usually threefold.

Retention of water. Leads to water intoxication. The maximum renal diuresis is about 1-500 ml hourly. When the renal arterial pressure is low as in post-haemorrhagic states this condition may easily arise. Nausea and vomiting represent an attempt at physiological correction: bradycardia, muscular twitchings, convulsions and coma are characteristic. Excess of water relative to extracellular electrolyte means that water can enter the cells: injection of hypertonic saline reverses this cellular invasion. Clinically water to slake thirst is harmless but intravenous and even rectal administration may be dangerous. The normal water requirement (by vein) is about 2 litres daily and if more liberal amounts are contemplated adequate electrolyte must be given as well. In anuria in adrenal cortical deficiency and post-operative states diuresis may be in abeyance and water harmful. Overdosage can be corrected by intravenous injection of 50-100 ml of 5 per cent sodium chloride.

solution and the use of a radiant heat cradle to promote sweating

Fluid replacement is therefore a problem in individual to each patient and laboratory data (plasma specific gravity potassium sodium or chloride and bicarbonate blood urea serum albumin) will give an indication of requirements. Physiological saline and glucose saline are useful up to a point beyond which solutions more adapted to the individual need must be substituted. For example if the sodium deficit exceeds that of chloride M/6 sodium lactate is an appropriate solution. Loss of gastric secretions should be compensated for by an acidic fluid whereas loss of bowel fluids indicates a replacement solution of basic composition.

Gastric containing 17 mEq potassium 63 mEq sodium and 150 mEq/litre chlorides the deficient cations being made up with ammonium.

Intestinal containing 12 mEq potassium 138 mEq sodium and 100 mEq/litre chlorides the excess of 50 mEq base being neutralised by lactate.

The ammonium and lactate are rapidly metabolised and the fixed ion content of these solutions resembles closely the fluids they replace. They are isotonic and may be given intravenously or subcutaneously.

Respiratory acidosis (low pH high CO_2 combining power acid urine) can be corrected by hypotonic saline and glucose or Ringer lactate intravenously. Chronic bronchitics were treated with acetazolamide (Diamox, Lederle) by J Nadell (1953) to reduce serum bicarbonate levels. Metabolic acidosis (low pH low CO_2 CP acid urine) if mild yields to Ringer lactate if severe Hartmann's solution or M/6 lactate should be given. Tetany may develop after treatment particularly in the presence of potassium deficiency which is relieved by Darrow's A lactate solution intramuscularly. Respiratory alkalosis (high pH low CO_2 CP alkaline urine) if mild responds to intravenous Ringer solution if severe N/4 ammonium chloride by vein is effective. For tetany intravenous calcium should be given. Metabolic alkalosis (high pH, high CO_2 CP alkaline urine) is treated by intravenous infusion of Ringer's solution physiological saline or if severe gastric solution.

Hypokalaemia An abnormality of the intracellular compartment and may exist without gross change in blood potassium levels. But in episodes of periodic paralysis caused by shift of potassium into the cells the serum potassium is low although no absolute deficiency of potassium exists nor clear relationship between paralysis and potassium level. This state of affairs may also present after dosage with insulin and glucose.

Sources of potassium are bread, meat and vegetables and restricted diets may induce hypokalaemia. As potassium has priority of excretion over sodium, the kidney continues to excrete it and it is depleted further by dehydration, by saline infusion, by the glucose diuresis of uncontrolled diabetes and by administration of adrenocortical hormones and testosterone. Loss of gastro-intestinal secretions is another important cause and replacement therapy which ignores potassium lack will obviously do harm. A fall in intracellular potassium induces apathy, muscular weakness and mental aberration—an altogether vague syndrome. Extracellular deficit on the contrary is easily detected and has characteristic signs: muscular paralysis of the ascending type leading to respiratory difficulty and generalised muscular weakness. The electrocardiogram shows flat or inverted T segments and depressed S-T segments. The Q-T interval is often prolonged but this is due to concomitant hypocalcaemia. A serum potassium level of under 4 mEq/litre indicates an extracellular deficiency; a normal does not exclude an intracellular deficit. Acidosis usually co-exists or alkalosis with high plasma bicarbonate levels.

Treatment If the kidney function is normal give 10-15 G potassium chloride daily by mouth (a mixture of the two phosphates is more palatable). If the kidneys are damaged the dose should be lower and controlled by serum potassium estimations. If oral dosage is impracticable give a 0.3 per cent (40 mEq/litre) solution of potassium chloride intravenously slowly (1 litre in three hours). The intramuscular route is safer. Reversal to a high voltage cardiogram is a sign of over-correction.

Intravenous potassium is dangerous unless there is a free diuresis; at in the oliguric state the outflow of potassium

from the cells may far exceed the capacity of the kidneys to excrete it and dangerous accumulation in the plasma will follow. Glucose facilitates the passage of potassium into the tissues and saline corrects dehydration and improves the urinary flow. Potassium if still required will then be safe.

Hyperkalemia May complicate Addison's disease, renal failure or intravenous potassium therapy. The signs are paraesthesiae, flaccid paralysis and electrocardiographic stigmata (absent T segment, widening of QRS and high voltage sharply peaked T segments). The danger level is 10 mEq/litre (about twice the normal figure). The most effective treatment is glucose and insulin. Oral administration of a sodium cation exchange resin (Resonium A, Bayer Products 45-60 G daily) is also helpful.

Electrolyte balance is an important consideration in treatment of anasarca by fluid and sodium restriction, mercurial diuretics and cation exchange resins. Dehydration and salt loss syndrome may develop in elderly cardiac patients. The blood urea level, although normal at the beginning of treatment, rises smartly and the plasma chloride falls, giving a disturbing clinical picture of apathy, somnolence, mental confusion and coma, leading to death. The anasarca is unresponsive or may increase. Hypochloræmic alkalosis usually supervenes, as indicated by elevated plasma bicarbonate and pH. The salt deficit should be calculated and replaced. Ringer's solution is satisfactory for this purpose.

In collective electrolyte therapy it should be borne in mind that biochemical tests are sometimes fallacious and must be interpreted in terms of clinical facts such as extent and mode of fluid loss. Over-correction must be avoided; the normal homeostatic capacity of the kidney will ensure fine adjustments, once major aberrations have been remedied.

CHAPTER XIII

DISEASES OF THE CARDIOVASCULAR SYSTEM

Pericarditis

Absolute rest in bed is essential and the patient may be propped up with pillows or bed rest if dyspnoea is severe. Diet should be restricted to fluids and bowel evacuation secured by salines or enemata. Precordial pain is a distressing feature which is met by kaolin poultices, icebags or short wave diathermy. Analgesics such as sodium salicylate and aspirin are indicated and full dosage is required in cases of rheumatic origin. Codeine, morphine and methadone are valuable remedies for severe pain, restlessness and insomnia. Dyspnoea and cyanosis become more pronounced with the advent of pericardial effusion and should be countered by continuous inhalation of oxygen by tent or suitable mask. Appropriate antibiotic therapy must be pushed if the pericardial infection is likely to be bacterial in type.

Many rheumatic cases never progress to the stage of effusion but if this complication arises further treatment will depend upon its extent. Small and moderate effusions cause little subjective discomfort whereas large collections of fluid induce a state of cardiac tamponade manifested by dysphagia, vomiting, increasing cyanosis and dyspnoea, rapid and irregular pulse with falling blood pressure. Paracentesis must be done. In cases following pneumonia, empyema or general septicaemia aspiration is necessary for bacteriological diagnosis. The choice of route is determined by the disposition of the exudate within the pericardium as judged by clinical and radiological features but trial and error is often the ultimate resort.

Purulent effusions are aspirated on alternate days and if the organism is penicillin sensitive 20,000 units in 2.5 ml of normal saline should be introduced after each aspiration and appropriate intramuscular dosage given. The broad spectrum

antibiotics are given orally when indicated by bacteriological findings. Some recover after aspiration and appropriate antibiotic therapy while others require surgical drainage and toilet of the pericardial surfaces.

ACTH and cortisone are of value in short history cases of rheumatic carditis. Dosage of the former (as H.P. Acthar gel Armour) is 50-100 I.U. intramuscularly daily for 4-6 days and then tapered if progress is satisfactory. Caution is necessary where an element of cardiac decompensation is present and methylprednisolone is safer (0.5 mg./lb. daily until the infection is controlled).

Streptokinase-streptodornase preparations facilitate removal of blood and pus from the pericardial cavity by aspiration. The first mentioned enzyme liquefies fibrin clots and the second inspissated pus.

All cases of pericarditis require four weeks rest in bed after active manifestations have passed. Prolonged convalescence is essential and the patient ought to remain under surveillance for a considerable period. Rheumatic and tuberculous subjects are given the long term observation and treatment appropriate to these infections. Pericarditis of viral origin is usually benign and requires treatment on general principles.

Pericardial Adhesions

Chronic Constrictive Pericarditis

Usually a sequel of tuberculous pericarditis.

Medical treatment includes restriction of physical exertion, and rest in bed when necessary. Ascites and oedema may be lessened by dietetic and diuretic measures. Cases showing extensive extrapericardial adhesions carry a gloomy prognosis in the absence of operative treatment. Localised thoracoplasty will reduce the myocardial burden and do much to prevent invalidism.

In the chronic constrictive variety mediastinal adhesions are absent but the fibrotic and calcified pericardial layers form a rigid blanket round the heart and great vessels. Pericardiectomy yields very successful results. The ventricles are widely decorticated but auricles and venæ cavae are cautiously freed. Operation should be considered just as soon

as the diagnosis of cardiac compression can be made clinically. Cyanosis distended neck veins small pulse volume low blood pressure large liver dry lungs and dropsy are suggestive. Active tuberculous effusion is not a contra indication to operative treatment but an indication for preliminary aspiration streptomycin cover and subsequent prolonged chemotherapeutic course.

DISTURBANCES OF CARDIAC RHYTHM

Premature Contractions

As a rule these require no treatment unless associated with major lesions. Occasional extrasystoles are of no significance but they may arouse considerable mental perturbation in introspective subjects. Reassurance is often the most important detail of therapy.

In more resistant cases gastric flatulence over eating tobacco alcohol and concealed dental sepsis are possible aggravating causes and the appropriate remedy should be advised. Drug treatment is often disappointing but one or other of the following may abolish the premature contractions.

Phenobarbitone gr $\frac{1}{2}$ -1 thrice daily

Quinidine sulphate gr 6 daily for ten to twelve days

Procainamide 0.25 G twice daily

Potassium acetate gr 45 nightly

Frequent or recurrent premature contractions suggest that the heart may be damaged or in the grip of a toxæmia or herald the advent of major arrhythmia (paroxysmal tachycardia or fibrillation heart block). Digitalis coupling is a signal for interruption of therapy and potassium dosage as above.

Paroxysmal Tachycardia

This may occur in apparently healthy hearts as well as in those affected by rheumatism myocardial infarction or thyrotoxicosis. In the idiopathic group a tendency to neurosis and hypertension is frequently present. The sudden onset of

rapid regular cardiac action (150-200 per minute) and its equally sudden cessation are characteristic. The attack may last for seconds or days and repetitive forms are common if the arrhythmia is prolonged signs of cardiac failure may supervene although the condition is seldom fatal.

Treatment varies according to the site of origin of the abnormal rhythm and electrocardiographic diagnosis is therefore a matter of importance.

Supranodal type. Deep barbiturate sedation may be effective alone and a mild hibernation cocktail is useful for repetitive and resistant cases. promethazine (Phenergan M & B) 25 mg, chlorpromazine (Largactil M & B) 25 mg, phenobarbitone gr $\frac{1}{2}$ three daily.

Vagal Stimuli

Methods: 1. Strenuous muscular effort during deep and prolonged inspiration. 2. Pressure on one or both carotid sinuses. The fingers should be applied to the carotid artery at the level of the mandibular angle and the artery compressed against the vertebrae. Several treatments of fifteen to thirty seconds duration may be necessary commencing with the right sinus. 3. Gagging reflex. Irritation of the pharynx with the finger or tooth brush. This is the most certain manoeuvre. Unfortunately these methods tend to lose their effectiveness on frequent repetition and recourse may then be made to emetics e.g. apomorphine gr $\frac{1}{8}$ hypodermic. tincture of ipecacuanha 2-4 drachms orally.

If the above measures are without avail the injection of parasympathetic-inhibiting drugs is often successful.

Neostigmine methylsulphate 1-1.5 mg intramuscularly and repeated once or twice at three hourly intervals.

Mechol n (Amechol Savory & Moore) 15-30 mg. intramuscularly.

Metformamine (Vasomax B.W.) 10-20 mg. into vein or muscle.

Licophonium chloride (Tension Roche) 40 mg. intravenously.

These drugs should not be given to asthmatic or cardiovascular degenerative subjects. They will often abort the

paroxysm within a few minutes and may be used in conjunction with carotid sinus pressure. If they cause untoward reaction atropine gr $\frac{1}{16}$ should be used intravenously. Frequent injection of these preparations may be harmful and their action by the oral route is uncertain.

Quinidine sulphate is sometimes valuable in resistant cases. It is best given in dosage of 0.3-0.5 G in 10 ml of normal saline into a vein. Mouth dosage is also useful gr $\frac{1}{2}$ two-hourly until the attack ceases (maximum five doses) but in prolonged paroxysms dosage of gr 12-16 two-hourly for three doses is more effective. Procainamide (Pronestyl Squibb) is of limited utility in auricular tachycardias. For dosage see below. For desperate cases where cardiac failure threatens a single intravenous digitalising dose of digoxin (1.15 mg) or lanatocid C (Cedilanid 1.16 mg) may restore normal rhythm. Carotid sinus pressure should be tried at intervals after the injection.

Some patients can maintain freedom from attacks by taking gr 3 of quinidine sulphate three daily and increasing until an effective dose is found. Procainamide 2-4 tablets daily is also worth trial.

Nodal type Usually responds to digitalisation.

Ventricular type Less common than the others but of more serious import as coronary occlusion may be the cause. Digitalis and choline esters should not be given as they may induce ventricular fibrillation. Quinidine sulphate is generally employed in initial dosage of 0.4 G intravenously followed by gr 6 by mouth two-hourly for one day. This usually causes gradual slowing of the idioventricular rate to a point where the more rapid sinus rate will become dominant. If unsuccessful twice this amount of quinidine should be given on the second day. Once sinus rhythm has been re-established dosage should be reduced to maintenance level.

Procainamide has a quinidine like action which has proved useful for treatment of cardiac arrhythmias. It will abolish premature contractions temporarily and is effective against digitalis bigeminy. The drug is more valuable in ventricular than auricular tachycardia. results in the nodal type are fair. Oral dosage is 3-5 tablets of 0.25 G followed by 2-4 tablets every four to six hours until normal rhythm appears. A 10

per cent. solution is available for use in emergency (intramuscularly 10 ml over ten minutes intravenously 2-4 ml over two to four minutes) Intravenous use is mainly for prevention or correction of arrhythmias presenting in course of intrathoracic operations. It may induce hypotension for which intravenous noradrenaline is required.

Potassium salts (acetate gr 45-90) should be given in cases associated with potassium lack or digitalis intoxication.

Heart Block

Possible aetiological factors should be considered and treatment planned accordingly. Syphilis is an occasional cause and calls for the antisyphilitic routine applicable to cardiovascular cases. Rheumatism and diphtheria are the commonest causes in young subjects. Here the heart block usually disappears when the primary lesion has stabilised. Bundle branch block is often a manifestation of myocardial infarction involving the interventricular septum.

Sino-auricular block mild degrees of auriculo-ventricular dissociation (increased PR interval or occasional dropped beats) congenital heart block and Wolff Parkinson White types have no adverse effect on cardiac function and require no special treatment. For high grade partial and complete auriculo-ventricular block the patient should be encouraged to live within his cardiac tolerance. Digitalis and quinidine are as a rule contra indicated in partial heart block unless cardiac decompensation is present. The former need not be withheld in established total A-V block. Attempts at diminution of auriculo-ventricular block are not conspicuously successful but the following may be tried.

Isoprenaline sulphate 20 mg. sublingually three daily

Ephedrine sulphate gr $\frac{1}{2}$ -1 twice or three daily

Methylamphetamine hydrochloride one to two 5 mg tablets daily

Prednisone has proved useful for A-V block of recent onset not due to coronary occlusion.

However treated, cases of high partial heart block tend to gravitate into the dangerous Stokes-Adams syndrome. Here

the best remedy is adrenaline 1 : 1 000 10-20 minims subcutaneously Hyperdunc adrenaline A & H 1 ml subcutaneously is also useful and the effect may be reinforced by administration of ephedrine by mouth Barium chloride and thyroid extract are disappointing Oxygen inhalation in high concentration is essential in severe cases to relieve cerebral anoxia For prolonged ventricular asystole the only resource is injection of 1-2 ml of adrenaline 1 : 1 000 into the right ventricle ventricular fibrillation is abolished by an electrical defibrillator current

S. Bellet gives 250 ml of M/1 sodium lactate by intravenous drip to increase the idioventricular rate and abolish Stokes-Adams manifestations

Intraventricular block Treatment is that of the associated myocardial lesion

Auricular Flutter

Scherf and Prinzmetal established the similarity of the mechanisms of the auricular arrhythmias—premature contractions, tachycardia and flutter

Paroxysmal flutter may occur in apparently healthy hearts Flutter may complicate rheumatic carditis and thyrotoxicosis it is not uncommon in coronary thrombosis and myocardial degeneration The ventricular rate varies from 140 to 300 per minute according to the degree of auriculo-ventricular dissociation present Cases with 2 : 1 or 3 : 1 A-V block often experience little inconvenience from this arrhythmia but anything which increases the ventricular rate may induce palpitation and dyspnoea

Many cases have an element of cardiac failure digitalis will slow the ventricular rate and full dosage should be given (see p. 216) Normal rhythm may ensue or more commonly the flutter is replaced by auricular fibrillation This in turn may disappear within a few days of cessation of digitalis therapy if not it may be abolished by quinidine treatment (see p. 218) An alternative method which is equally successful is to secure preliminary slowing of the ventricular rate by moderate doses of digitalis and then correct the flutter with quinidine Another useful method for cases in which prompt relief is required is to give 0.8 mg. of a lanatocide C preparation intravenously and repeat in four hours Reversion to

sinus rhythm may follow quickly if not the drug is continued in daily dosage of 1 mg. Fibrillation frequently supervenes and this is an indication for change to quinidine.

Paroxysmal flutter usually responds to sedation or to full doses of quinidine or procainamide.

Atrial Fibrillation

May occur in paroxysms without evidence of cardiac defect. This arrhythmia is sometimes an expression of acute myocardial intoxication as in erysipelas and thyrotoxicosis. The most common origin is in mitral stenosis but it frequently heralds the terminal phase of hypertension and decreascent cardiopathy. It is not uncommon in myocardial infarction and constrictive pericarditis.

In the acute fibrillations of toxic states such as exophthalmic goitre the primary condition must receive appropriate attention. Once thyrotoxicosis is controlled by antithyroid drugs the fibrillation tends to disappear if not quinidine therapy will usually prove successful. Fibrillation accompanying acute infections in elderly subjects is difficult to control. If endangering life by cardiac failure intravenous digoxin or strophanthidin dosage is indicated. Atrial fibrillation complicating coronary occlusion is often unresponsive to treatment but if a rapid ventricular rate persists in spite of the usual coronary treatment full dosage of quinidine should be tried. Digitalis alone is said to increase the risk of inducing ventricular fibrillation but simultaneous administration of quinidine appears to offset this effect.

In paroxysmal fibrillation precipitating factors such as overstrain, focal infections, dietary indiscretions and excessive use of alcohol and tobacco may often be recognizable and freedom from attack will follow their discontinuance. In cases where the paroxysms are infrequent prompt sedation, with internal treatment by a tranquilliser like benactyzine (Savril 150 dose 1-3 mg daily) may prevent them. A more persistent frequently recurring or resistant attack should be treated by a full course of quinidine sulphate orally followed by maintenance dosage of gr. 3 twice or three daily. Digitalis

must not be used on account of its liability to perpetuate the arrhythmia

Many patients of the decreascent type with long standing slow auricular fibrillation enjoy fair health and the advent of cardiac decompensation may be postponed by the institution of a rational régime rather than by drug treatment. Young rheumatic subjects with grossly damaged hearts do not stand fibrillation so well and there is little prospect of reversion to normal rhythm. Here the aim should be to delay the advent of cardiac failure or mitigate its effects.

If the fibrillation is of comparatively recent onset and there are no signs of gross cardiac damage an attempt should be made to restore normal rhythm.

Digitalis The most generally useful drug in auricular fibrillation. It slows the ventricle thus improving cardiac efficiency and normal rhythm may then be regained. For cases showing evidence of cardiac decompensation and without digitalis medication within twenty days the drug should be administered in full dosage.

Digitalis leaf tablets are reliable in action, economical and convenient. Leaf is often better tolerated than more active preparations in maintenance therapy. Gr 15 of leaf (0.1 G) is equivalent to 15 minims (1 ml) of tincture. The initial digitalising dose is gr 9 on the second day gr 6 and maintenance is gr 3.

Digitalin (digitoxin) is a glycoside of *D. purpurea* which is unique in its rapid and complete absorption from the bowel and slow elimination. As the effects of oral and intravenous administration are similar the latter offers no advantage except where vomiting is troublesome. Tablets of 0.1 mg (gr $\frac{1}{10}$) equal to 10 minims of tincture and 0.25 mg (gr $\frac{1}{4}$) equal to 25 minims are available. The digitalising dose = 1.15 mg and the maintenance dose approximately 0.25 mg daily.

Digitalis lanata The representative glycoside lanatocide C is of uniform potency and does not require biological standardisation. Another practical advantage is that being crystalline and soluble it is suitable for intravenous use. It is more rapidly absorbed and excreted than the glycosides of *D. purpurea* and is therefore less likely to cause

accumulation symptoms. Cedilanid Sandoz, is pure lanatocide C and is available in tablets of 0.25 mg. and ampoules of 0.4 mg. The oral digitalising scheme ■

1st day	2nd day	3rd day	maintenance
3.5-6 mg.	2.5 mg.	1 mg.	0.75-1.25 mg.

Digoxin is a product of lanatocide C hydrolysis and is the most popular digitalis preparation in this country. Tablets of 0.25 mg. (equivalent to 1 ml. of tincture) solution containing 0.5 mg. per ml. (equivalent to 2 ml. of tincture) and ampoules for intravenous use containing 0.5 mg. are available. The initial dose for a subject weighing 140 lb. is six tablets followed by two tablets four hourly for six doses then one tablet four times daily. Maintenance dose is one to three tablets daily.

Strophanthus, has no advantage over digitalis for oral medication but its glycosides act rapidly on intravenous injection. Strophanthin is a mixture of amorphous glycosides, and it is useful for cardiac emergencies in dosage up to gr. $\frac{1}{2}$.

Strophosid Sandoz, a crystalline glycoside of strophanthin, is of constant potency dose 0.5 mg. by vein.

Intravenous medication is reserved for cases (without digitalis during the previous four weeks) of urgent cardiac defeat where immediate action is desired or where oral dosage is precluded on account of vomiting. Any of the under mentioned preparations may be used.

Solutions of

Cedilanid Sandoz
or Digoxin
0.5-0.75 mg.

Strophanthin
gr. $\frac{1}{2}$

These should be diluted to 10 ml. with normal saline and given slowly into a vein taking care to avoid spillage into the perivascular tissues. The initial dosage may in grave emergency be double these amounts or the above may be repeated in three or four hours. Oral dosage as at the second stage e.g. one-eighth of the digitalising dose of tincture or two tablets of digoxin four-hourly or 2.5 mg. of Cedilanid in twenty-four hours should be commenced as soon as practicable.

1 AIDS TO MEDICAL TREATMENT

can not be used on account of its liability to perpetuate the arrhythmia.

Some patients of the decompensated type with long standing heart failure at first enjoy fair health, and the advent of cardiac decompensation may be postponed by the institution of a medical regime rather than by drug treatment. Young patients with hearts and freshly damaged hearts do not stand heart failure so well, and there is little prospect of reversion to normal rhythm. Here the aim should be to delay the advent of cardiac failure or to give its effects.

If the situation is of comparatively recent onset and there is no sign of gross cardiac damage as a rule should be made to resuscitate the heart.

Digitalis. The most generally useful drug in cardiac failure is digitalis. It slows the ventricle thus improving cardiac efficiency and normal rhythm may then be regained. For cases showing evidence of cardiac decompensation and without digitalis medication within twenty days, the drug should be administered in full dosage.

Digitalis leaf tablets are reliable in action, economical and convenient. Leaf is often better tolerated than more active preparations such as the tincture. 0.5 g of leaf (0.1 G) is equivalent to 15 minims (1 ml) of tincture. The initial dosing dose is $gr\ 9$ on the second day $gr\ 6$ and maintenance is $gr\ 3$.

Digitalin (0.5 g oral) is a glycoside of *D. purpurea*, which is absorbed in the small intestine and absorbed from the bowel and its elimination. As the effects of oral and intravenous administration are similar the latter offers no advantage except where vomiting is troublesome. Tablets of 0.1 mg (gr 1/10) equal to 10 minims of tincture and 0.25 mg (gr 1/16) equal to 25 minims are available. The digitalis dose is 1 to 3 mg and the maintenance dose approximately 0.25 mg daily.

Digitalis laurifolia. The representative glycoside lanatoside C_{42} is of superior potency and does not require biological standardization. A other practical advantage is that being crystalline and soluble it is suitable for intravenous use. It is more rapidly absorbed and excreted than the glycosides of *D. purpurea* and is therefore less likely to cause

accumulation symptoms. Cedilanid Sandoz, is pure lanatocide C, and is available in tablets of 0.25 mg. and ampoules of 0.4 mg. The oral digitalising scheme is

1st day	2nd day	3rd day	maintenance
3.6 mg	2.5 mg	1 mg	0.75-1.25 mg

Digoxin is a product of lanatocide C hydrolysis and is the most popular digitalis preparation in this country. Tablets of 25 mg. (equivalent to 1 ml. of tincture) solution containing 5 mg. per ml. (equivalent to 2 ml. of tincture) and ampoules or intravenous use containing 0.5 mg. are available. The initial dose for a subject weighing 140 lb. is six tablets followed by two tablets four hourly for six doses then one tablet four times daily. Maintenance dose is one to three tablets daily.

Strophanthus. Has no advantage over digitalis for oral medication but its glycosides act rapidly on intravenous injection. Strophanthin is a mixture of amorphous glycosides and it is useful for cardiac emergencies in dosage up to gr. $\frac{1}{2}$. Strophanthid Sandoz a crystalline glycoside of strophanthin is of constant potency dose 0.5 mg. by vein.

Intravenous medication is reserved for cases (without digitalis during the previous four weeks) of urgent cardiac defeat where immediate action is desired or where oral dosage is precluded on account of vomiting. Any of the under mentioned preparations may be used.

Solutions of

Cedilanid Sandoz
or Digoxin
0.5-0.75 mg

Strophanthin
gr. $\frac{1}{2}$ -

These should be diluted to 10 ml. with normal saline and given slowly into a vein taking care to avoid spillage into the perivenous tissues. The initial dosage may in grave emergency be double these amounts or the above may be repeated in three or four hours. Oral dosage as at the second stage e.g. one-eighth of the digitalising dose of tincture or two tablets of digoxin four hourly or 2.5 mg. of Cedilanid in twenty four hours should be commenced as soon as practicable.

The above mentioned cardiac drugs are all reliable and selection is largely a matter of personal preference. The practitioner should familiarise himself with the action of two or three preparations. Digoxin tablets and ampoules and digitalin tablets comprise an adequate armamentarium for most problems in digitalis therapy.

Digitalis intoxication. Minor manifestations (anorexia, nausea, vomiting) respond to temporary reduction or cessation of dosage, gastric sedatives and a few oral doses of chlorpromazine. In severe digitalis intoxication (multifocal ventricular ectopics, bigeminy, ST-T deformity, sino-auricular or auriculo-ventricular block, auricular fibrillation, paroxysmal auricular tachycardia) the glycoside must be discontinued for several days after all evidence of toxicity has disappeared. Potassium salts are protective and intoxication is readily induced in hypokalaemic states (following diuretic or corticosteroid therapy, anorexia and defective potassium intake). For major arrhythmias potassium citrate should be given in dosage of 4 G in fruit juice followed by two doses of 2 G at two hourly intervals. The intravenous route is more effective (3 G potassium chloride in 500 ml 5 per cent glucose at the rate of 5 ml per minute. Stop as soon as the arrhythmia disappears). For paroxysmal ventricular tachycardia unresponsive to potassium, procainamide should be tried (750 mg orally followed by 250 mg hourly for three doses; if oral dosage not retained give 0.5 ml of a solution containing 100 mg per ml every two minutes in an intravenous drip to a total of 300 mg followed by 50 mg every four minutes until 1 G has been given). If the blood pressure falls, noradrenaline should be substituted. Intravenous therapy should be monitored electrocardiographically.

Quinidine. Digitalis acts by improving the peripheral circulation and myocardial nutrition. It also increases auriculo-ventricular block and these effects are beneficial in fibrillation but no radical influence is exerted on the abnormal auricular conduction pattern. Quinidine has a more direct action and may damp down the rate of discharge from ectopic auricular foci or improve auricular conductivity.

In a successful case the auricular fibrillary movements are replaced by effective contractions and there is danger of auricular appendicular clots being expelled into circulation. This danger has been overrated but it is customary to prescribe a preliminary two to three weeks anticoagulant course.

Quinidine acts best in fibrillation of recent onset and in young rheumatic subjects rather than in elderly arteriosclerotics. Gross valvular defect, cardiac enlargement and the presence of decompensation are almost certain guarantees of failure. It will often succeed temporarily in borderline cases but the advantage thus gained is doubtful. Quinidine therapy gives brilliant results in a carefully chosen minority of fibrillators but digitalis is the drug of choice for the majority. Milder examples often regain normal rhythm under its influence. In more advanced cases the myocardial inadequacy element can be controlled and quinidine may then be used with enhanced prospects of success.

Idiosyncrasy within six hours to a gr 3 dose in the form of headache, tinnitus, gastro-intestinal disturbance or skin rash and development of intraventricular block at any time are indications for discontinuance of the drug. Gr 3 tablets or powders are given three daily and the dose increased by gr 3 daily until the pulse becomes regular or a maximum of gr 48-60 daily is reached. If necessary the maximum dosage may be gr 7½ two-hourly for twelve doses. In successful cases the dosage is replaced by a maintenance one of gr 6-9 daily for weeks or months. If however relapse is to be feared the successful dose should be tapered by gr 3 daily until the maintenance level is reached. An excellent alternative method is to give quinidine gr 6 two-hourly for five doses daily over a maximum period of seven days. Dosage need not cease if flutter supervenes.

Effective quinidine therapy will increase the pulse rate and may provoke ventricular tachycardia. It is therefore a most desirable preliminary that the pulse rate be reduced to near normal by digitalis and sedatives.

Ventricular Fibrillation Cardiac Arrest

May appear as an aërial phenomenon. It is a troublesome complication of general anaesthesia and thoracic

operations and may herald the beginning or end of cardiac standstill in Stokes-Adams seizures

Quinidine is the best remedy for the paroxysmal variety and when cardiac infarction is present. In cases arising during anaesthesia prompt treatment is necessary to avert cerebral and myocardial anoxia which may prove fatal. Adequate oxygenation should be maintained by artificial respiration using 100 per cent oxygen and quinidine given intravenously. Cardiac massage through the open pericardium will provide a minimal circulation. If the thorax is already open this should be diverted to the areas of greatest need by compressing the aorta below the origin of the carotids. The arrhythmia can be abolished by passage of small direct currents through the ventricular muscle mass and a simple apparatus has been described by Burnbaum, McMullan and others. The first named uses a preliminary injection of 5 ml of 1 per cent procaine into the right and left ventricles and this is massaged into the coronary circulation. The defibrillator current (100 V 2 amps 50-60 c A.C. for 0.1-0.2 sec) is then applied several times. Momentary ventricular arrest follows adequate shocking which is usually replaced by normal ventricular activity if not the routine mentioned below must be instituted.

Cardiac standstill is another unpleasant anaesthetic complication the treatment of which is oxygenation and rhythmic compression of the heart from apex to base. If not effective 2 ml of 1:1000 adrenaline should be injected into the right ventricle and manual compression repeated. When cardiac contraction has been re-established the blood pressure should be supported by an intravenous drip containing noradrenaline 4 mg or methoxamine (Vasoxin II W) 20-40 mg.

An artificial pacemaker delivers a spot current to the region of the sino-auricular node. This method has proved effective in abolition of cardiac asystole.

Pulsus Alternans

Not an arrhythmia but an expression of myocardial exhaustion. Digitalis should not be withheld if signs of cardiac decompensation are present.

Acute Carditis

Usually a complication of acute rheumatism scarlet fever or streptococcal tonsillitis. Treatment is in general that of the causal condition. All measures calculated to improve nutrition should be taken including the provision of a liberal and nourishing dietary. Cortisone and the daltasteroids appear to have a useful rôle in rheumatic carditis (see p. 50). When the febrile stage has passed fish liver oil and iron tonics are of value. Prolonged and complete rest must be ensured. During warm weather the child may be carried or wheeled to a balcony or garden and such hobbies and educational pursuits as are compatible with physical rest will prevent tedium. Massage and exercises for the limb muscles help to maintain morale and body tone.

There is no advantage in over prolonging the bed rest. When the temperature, pulse rate and blood sedimentation rate have remained normal for some weeks and the cardiac condition appears to be stabilised the patient should be allowed to sit up in a chair. In a few days he is given the freedom of his bedroom or balcony for half an hour. If no disturbance of the pulse rate results further increments of activity are allowed. Dyspnoea, palpitation and increased pulse or sedimentation rate are indications for temporary curtailment of physical exertion. A prolonged holiday in the country or at the seaside will do much to rehabilitate the rheumatic child. Cardiac colonies where they may live and receive education under ideal conditions are a noteworthy contribution to the problem.

Periodic re-examination and after-care are necessary for several years. Streptococcal infections of the upper respiratory tract should be warded off by long term penicillin therapy (see p. 51).

Infective Endocarditis**Subacute Bacterial Endocarditis**

All measures designed to conserve strength and increase resistance should be exploited. Complete rest in bed, nourishing food with vitamin supplements, fresh air and sunshine are desirable. Transfusions of blood or packed cells are the most satisfactory remedy for anaemia.

The ætiology of the case may provide indications for treatment. Those arising from metastatic infection should have appropriate treatment of the primary focus. Where the endocardial infection is superimposed on a patent ductus arteriosus the ductus should be tied after a preliminary course of antibiotic therapy.

Penicillin is the most generally effective antibiotic in infective endocarditis. Sensitivity titres are a useful guide to dosage. If the infecting organism is sensitive to this drug (the infecting organism is *Str. viridans* in 90 per cent of cases and 90 per cent of these are sensitive) a thirty to forty days course of 2 mega units of crystalline penicillin daily by 6-hourly intramuscular injection should be given. If the response is rapid and progress uninterrupted procaine penicillin (600 000 units twelve hourly) may be substituted during the latter part of the course. In most cases defervescence is complete and the blood stream sterile within one week but if partial response is shown after a few days treatment penicillin dosage should be increased to 5-10 mega units daily over a period of forty to fifty days. Relapse usually manifests itself within a month and should be combated by heavier antibiotic dosage. Where the infecting organism is relatively insensitive to penicillin one of the tubular blockade drugs should be used in addition to liberal penicillin dosage. Probenecid (Benemid, Merck, Sharp & Dohme) is the most effective of the group and 0.5 G should be given six hourly by mouth. It has no effect on streptomycin levels. Oral penicillin has given good results in bacterial endocarditis but it should not be depended upon in the first instance.

Some *Str. viridans* and many *Str. faecalis* and *H. influenza* strains show poor response even to heavy penicillin dosage for these a combination of penicillin and streptomycin is often effective. 6 mega units and 1.2 G daily being a representative dose. This combination has the advantage of bactericidal action whereas broad spectrum antibiotics are bacteriostatic only and may prove disappointing even when indicated by sensitivity tests.

The tetracyclines and chloramphenicol are of value in occasional cases in which the organism shows insensitivity

to penicillin and streptomycin coupled with sensitivity to one of the newer antibiotics. Relapse is frequent and dosage should be in the region of 3.6 G daily over forty five days or longer if necessary. If gastro-intestinal upset precludes adequate oral therapy chlortetracycline and oxytetracycline can be administered by vein for some days (600 mg twelve hourly) chloramphenicol is reasonably well tolerated intramuscularly or intravenously (600 mg six hourly). This will permit of lower mouth dosage. The tetracyclines and erythromycin have particular virtue in staphylococcal infections whereas chloramphenicol may be the agent of choice in infections due to Gram negative organisms. Neomycin, bacitracin, polymyxin and the nitrofurans have certain narrow indications in bacterial endocarditis.

Since the advent of antibiotics the mortality of this disease has fallen from 97 per cent to under 30 per cent. Delayed diagnosis is a factor in the still substantial death rate and it is unfortunate that bacteriological diagnosis is sometimes difficult or impossible. The disease should be thought of in every case with a cardiac lesion and fever persisting over one week. Elderly men with prostatic obstruction often have unsuspected enterococcal endocarditis.

Chronic Valvular and Myocardial Lesions

During the stage of *compensation* no active treatment is required. The severity of the lesion and the cardiac reserve should be estimated and the patient's mode of life altered if necessary in conformity with cardiac tolerance. The danger of engendering a needless atmosphere of invalidism should be avoided. Within the rule of moderation he should be allowed to live as full a life as possible. If the occupation is suitable he may be encouraged to continue with it but ample leisure and relaxation must be arranged for. Any recreation in which he can indulge without appreciable discomfort is beneficial. The patient's habits regarding diet, alcohol and tobacco are reviewed and moderation imposed. Reasonable precautions should be taken to prevent colds, chills and upper respiratory infections. When such occur they must be treated with respect.

bedtime is good in elderly patients as it reduces their sedative requirements. The paroxysm can be cut short by oxygen inhalation and an intravenous dose of aminophylline. The latter will abolish Cheyne Stokes respiration temporarily.

Cardiac edema. Adequate digitalization is of prime importance in the dissipation of dropical collections. Removal of pleural and peritoneal transudates by paracentesis will relieve dyspnoea and expedite recovery of water balance. For massive edema of the lower limbs multiple skin puncture with a glove needle (under aseptic precautions) is of great assistance. If possible, the patient should be seated in a chair with the feet in a basin during the drainage process. If skin puncture must be done with the patient recumbent mackintosh sheets are arranged under him so as to provide drainage into a basin on the floor. Southey's tubes used in the same way are much more efficient as the needle punctures tend to seal with clotted serum. Edema of the scrotum and prepuce causes extreme discomfort and skin punctures should be done under anidiosis cover.

Comprehensive mechanical drainage with frequent changes of posture and adequate diuretic medication may be sufficient to prevent re-collection of dropsy if not further measures must be employed. We have found a modified Schemm's routine valuable in cardiac oedema with reasonably good renal function. The intake of sodium is restricted and reasonable fluid allowed. Salt is omitted both in cooking and at table and sodium salts are not ordered in prescriptions. The insipidity of this diet can be cloaked to some extent by the use of flavourings like lemon juice, vinegar, pepper etc. In a few days a satisfactory diuresis occurs with reduction of oedema. If renal function is not grossly impaired merzalyl may be used to control dropsy. A test dose of 0.5 ml. should be given intramuscularly and if without untoward effect injections of 1-2 ml. are given at intervals of four to seven days according to requirements. Toxic manifestations are more likely to follow intravenous than intramuscular administration. dimercaprol (BAL) is the best antidote (three 4 ml. doses of 5 per cent oily solution at intervals of 3-4 hours into a muscle). Oral dosage with ammonium chloride gr 15-20 in 5-6 wine or capsule four times daily will enhance the

diuretic action of mersalyl provided renal function is intact and the administration of this drug should commence on the day preceding and be continued for a day after each injection. We have found mersalyl injection on two consecutive days in each week more effective than single doses at four day intervals. The drug is disappointing if used in tablet or suppository form and the latter is not free from the danger of chemical proctitis. Mercaptomerin sodium (Thiomerin Wyeth) is reputed to be less nephrotoxic than mersalyl. In similar dosage it is equally effective in a more leisurely fashion.

The tablet diuretic group includes acetazolamide Diamox, Lederle dose $1\frac{1}{2}$ tablets on alternate days, amosmetradine Rolicton, Searle dose 4 tablets on the first day and then 2 tablets daily or more if required, chlorothiazide Saluron, Merck Sharp & Dohme is an effective oral diuretic which like amosmetradine increases sodium chloride excretion by the kidney dose 1-4 tablets on the first day followed by 1-3 tablets daily on two to five days weekly according to response. They are useful adjuvants or alternatives to mercurials being non toxic. These are particularly acceptable for maintenance once heavy anasarca has been dissipated. Chlorothiazide reduces potassium levels thus potentiating digitalis the effect of hypotensive agents is also increased.

Cation exchange resins possess the property of selective absorption of inorganic ions and the acidic resins of carboxylic or sulphonic type will release hydrogen ions in exchange for sodium and potassium ions during transit through the intestine. Their action is mainly to prevent absorption of dietary sodium, but urinary output of this cation may be increased also. Their affinity for sodium is comparatively slight and unless modified by preliminary treatment with potassium they may induce hypokalaemia and hypocalcaemia with compensated acidosis. Katonium, Bayer Products (ammonium potassium sulphonic resin) may be given in dosage of 15-40 G daily in milk or fruit juice. Initial diuresis is usually satisfactory but may not be maintained and some patients become intolerant of the large bulk. They are occasionally useful as temporary alternatives to

mercurial diuretics particularly in cases where the latter tend to lose their effect. Some relaxation is allowable as regards the intake of dietary sodium during resin therapy.

The danger of induced hypochloræmic alkalosis in patients on a prolonged low sodium-diuretic régime has already been stressed (page 207).

The xanthine group have a most uncertain diuretic action but may be helpful if used alternately with mercurial diuretics. Theophylline ethylene diamine (aminophylline) is the most effective member of this group. Dosage by mouth 0.3 G three to five times daily (liable to cause gastrointestinal irritation) intramuscularly or intravenously 0.25-0.5 G.

Left ventricular failure. An acute emergency characterised by paroxysmal dyspnoea, pulmonary œdema and cyanosis or pallor. Hypertension and myocardial infarction are common antecedents.

The patient should be propped up in the sitting posture and morphine gr $\frac{1}{4}$ injected intravenously to allay nervous excitement. Venesection up to 20 oz should be done and aminophylline given by slow intravenous injection in dosage of 0.5 G dissolved in 10 ml of normal saline or better in 50 ml of 50 per cent glucose solution. Oxygen inhalation should be given preferably from a positive pressure machine in hope of limiting pulmonary alveolar exudate. While preparations for venesection are being made a nitroglycerin tablet of gr $\frac{1}{128}$ is given sublingually. This diminishes venous return to the heart by increasing the splanchnic reservoir action and the same effect may be obtained by applying sphygmomanometer cuffs to all four limbs and inflating them to 50 mm for thirty minutes. They should be released in rotation for ten to thirty seconds at intervals of five minutes. Tolazoline hydrochloride (10 mg slowly intravenously) is a useful emergency measure by reason of its rapid vaso dilator effect. A hexamethonium salt e.g. bromide 25 mg intramuscularly will rapidly ease the left ventricular burden in hypertensive subjects and has largely displaced tourniquets and nitroglycerin.

Full digitalising therapy must be proceeded with and the intravenous route is usually imperative.

DISEASES OF CARDIOVASCULAR SYSTEM 249

Cor pulmonale Right ventricular failure May present with cardiac abnormality such as pulmonary stenosis or with lung diseases like bronchitis emphysema embolism and fibrosis Pulmonary hypertension is a constant finding Severe dyspnoea cyanosis venous distention hepatomegaly and anasarca are usually marked

Treatment is that of congestive cardiac failure in general Bed rest light diet sodium restriction and aminophylline are beneficial Digitalis is often not dramatically successful but never harmful Diuretics especially mersalyl are an important item of treatment Oxygen inhalation is urgently necessary but some cases respond poorly due possibly to the respiratory centre having lost its sensitivity to CO₂ and responding only to oxygen lack Such cases should have oxygen intermittently by nasal catheter at first and be introduced gradually to the tent Dangerous hypoxic coma must be met by use of an intermittent positive pressure apparatus and intratracheal intubation using 5 per cent CO₂ in oxygen Venesection is theoretically contra-indicated as the high cardiac output and polycythemia are compensatory but in practice many patients feel relief after removal of 10-15 oz of blood Sedatives are usually required and if possible a barbiturate or Pethidofan Roche should be given in preference to morphine

Thrombo-embolic incidents in the course of cardiac decompensation serve to remind the practitioner of the fact that the precipitating factor in many cases is unrecognised myocardial infarction Where this possibility arises the prothrombin activity should be studied and anticoagulants used if indicated

For desperate cases of cardiac defeat radioactive iodine has been given in order to reduce metabolism and the cardiac load It is contra-indicated if the radioiodine uptake is below normal

When the stage of convalescence is reached diet may be increased The patient is allowed up for gradually lengthening periods and eventually may resume such activities as are considered suitable He should spend ten hours in bed out of each twenty four and the adoption of a regular rest day in each week will contribute to his well being He should

take sufficient digitalis and diuretics to ward off further episodes of cardiac decompensation

Surgical treatment Enormous strides have been made in the technique of valvuloplastic operations. Mitral valvotomy is now an accepted routine in suitable cases. Mitral stenoses may be classified into

- 1 Asymptomatic cases who do not require operation but should be kept under observation
- 2 Those who are well but have effort dyspnoea and usually show pulmonary hypertension
- 3 Cases in early failure (mitral facies, dyspnoea on slight exertion, moist signs at the lung bases) or with history of episodic failure
- 4 Cases of auricular fibrillation, established failure, embolism

Best results are obtainable in groups 2 and 3; in the latter invalidism can be averted by carefully timed valvotomy. Cases in group 4 are poor risks, but in view of the gloomy prognosis operation is justifiable provided that the patient can be brought to a state of reasonable cardiac competence.

Contra indications to mitral valvotomy. The most suitable age group is 20-40. Younger patients are liable to further rheumatic activity. Patients in the early fifties have undergone the operation successfully. Large left ventricle (aortic disease) or auricle (mitral incompetence). Minor degrees of reflux are not absolute contra indications. Active endocarditis, rheumatic or bacterial. Patients in the last trimester of pregnancy.

Brock's manoeuvre of splitting the valve commissure by finger pressure or valvulotome through an auricular appendage incision is the operation of choice.

The results of mitral commissurotomy have been surprisingly good. In a series of fifty cases reported by Brock there were eight deaths, seven of which occurred in the first twenty and one in the last thirty. Cases in groups 3 and 4 show a higher mortality, but the improvement in those who survive is sometimes remarkable. The long term prospects cannot yet be vouched for; a certain proportion of cases suffer restenosis and require further operation.

Valvotomy of the left ventricle or aorta is done routinely for relief of non-calcific aortic stenosis and stenotic pulmonary and tricuspid valves have been successfully incised.

Heart disease and pregnancy Pregnancy and parturition throw added burdens on the myocardium and kidneys. In the presence of a serious lesion such as mitral stenosis fatal congestive failure may be precipitated. Women with asymptomatic cardiac lesions may undergo several pregnancies without incident and many mitral stenotics are first discovered at routine antenatal examination.

Management of cases with a history of previous cardiac decompensation and of those showing signs of cardiac insufficiency early in pregnancy depends upon individual circumstances. With continuous medical supervision and rest, digitalis and an expeditious labour the outcome may be satisfactory. If the patient's environment is poor and the cardiac history bad, termination of pregnancy before the twelfth week may be desirable. Termination at a later stage is no less hazardous than normal labour and pregnancy should be allowed to proceed, the patient meanwhile receiving cardiac therapy and as much rest and freedom from domestic responsibility as possible. If labour is likely to be prolonged, rupture of the membranes and forceps extraction may be desirable; caesarean section is safer for primigravidae and it affords opportunity for sterilisation if strongly indicated. Cardiac decompensation must be corrected before any obstetrical procedure is contemplated. A mitral stenotic with history of previous cardiac embarrassment should, if possible, have a valvotomy between the fourth and eighth month.

Personal and psychological consideration should be carefully weighed before deciding the course of treatment. Many cardiac patients withstand pregnancy and labour surprisingly well, but repeated pregnancies may take heavy toll.

Arteriosclerosis

Degenerative arterial change is an hereditary and irreversible process, but under careful management such patients may enjoy years of useful and happy existence. Freedom from mental and physical strain is important, but a light and

congenial occupation is beneficial. Adequate rest and suitable outdoor exercise are to be encouraged and, if possible, a rigorous climate should be forsaken for an equable one.

Rigid dietetic extremes are unnecessary but moderation in food, drink and tobacco should be enjoined. The obese patient will benefit from a strict reduction régime. Simple fare including one meat dish daily may be allowed. Fatty foods, butchers' offals, fish roes, game, meat extracts and soups made with meat stock should as a rule be eschewed and salt intake restricted. There is considerable circumstantial evidence linking excessive dietary fat and arteriosclerosis. Atheromatous plaques contain large amounts of cholesterol. Present day dietetic tendency is toward hydrogenated fats and a high intake of saturated fatty acids connotes high levels of blood lipoproteins, whereas consumption of unsaturated fats (vegetable and certain fish oils) is associated with low levels of serum lipoproteins. Recent cardiac infarction subjects show high levels of plasma β lipoproteins. Keys has noted the much higher incidence of vascular degeneration in Americans whose national dietary is rich in animal fat as compared with the olive oil and pasta habit of Italian pastoral communities. The evidence is still inconclusive but it would seem worth while to reduce the intake of animal fat and eggs.

Drugs are without effect on the arteriosclerotic process but iodide had some reputation for symptomatic relief. Vertigo and insomnia are lessened by phenobarbitone gr $\frac{1}{2}$ 1 twice daily or by Phenobarbitone and Theobromine Tablets B.P.C. one three daily. Syphilitic taint should be eradicated by the methods recommended for cardiovascular syphilis.

When myocardial failure or vascular accident supervenes appropriate treatment should be instituted.

Syncope Vasovagal Attacks

Fainting attacks may have a psychological basis—a dramatic escape from unpleasant situations and some are frankly hysterical. These are responsive to psychotherapy.

Hypotensive syncopal incidents may arise from various causes and the vasodepressor type is common. Here the fall in blood pressure is due to vasodilatation in the muscular bed with constriction of the skin vessels and without compensatory increase in cardiac output owing to diminished venous return hence a critical level of cerebral hypoxia prevails. Emotion, fatigue, anaemia and painful sensory stimuli are exciting factors. Orthostatic hypotension may induce syncope without general autonomic disturbance and may be precipitated by starvation, illness or exhaustion.

Immediate treatment of hypotensive syncope is to place the sufferer recumbent with the head lower than the feet. A hypodermic injection of adrenaline is effective if the attack is prolonged. Recurrent syncope calls for complete physical examination; if findings are negative benefit will follow general tonic treatment and small doses of ephedrine.

The carotid sinus syndrome is found in elderly arteriosclerotics. Turning the head abruptly, wearing a tight collar or the presence of a carotid body tumour may evoke attacks by irritating a sensitive sinus. Sensitivity can be tested for by careful digital compression of each sinus in turn and the resultant attack may be abolished by injection of atropine. Frequent attacks lead to invalidism and denervation of the more sensitive sinus is indicated. A carotid tumour if present should be excised.

Fainting due to other causes e.g. paroxysmal cough from laryngeal irritation or mediastinal compression, hypoglycaemia, hyperadrenalism should have treatment of the primary lesion.

Arterial Hypertension

Usually associated with the degenerative changes common in middle life although vasospastic hypertension without appreciable vascular change is not rare. Hereditary influences are often recognisable. Cases occurring in various age groups may originate in a surgical kidney (or α radiation of these organs). Cushing's syndrome or pheochromocytoma and hypertension proximal to the block is a constant finding in adult aortic coarctation. Such cases are usually but not

invariably amenable to surgical treatment. In the vast majority the cause is not known and the therapeutic edifice rests on unsound foundations.

Many moderate hypertensives are symptom free, the condition being discovered on routine examination. Unless weighty reasons exist to the contrary, the patient should not be informed and nothing more than general modifications in his routine advised. Such a patient's life can be made miserable by induced neurosis if his abnormality is thoughtlessly exalted into a malady.

By adoption of a quiet and regular mode of life, the hypertensive may live comfortably with his disease for years; those showing evidence of gross renal defect have such poor prognosis that little is to be expected from treatment.

The sufferer should learn the secret of mental and physical relaxation and all treatment must be interlarded with practical psychotherapy designed to achieve this end. Business and professional pursuits should be on a reduced scale and confined to such interests as can be supervised without undue mental or physical stress. Diet and general routine are as for arteriosclerosis; correction of obesity is important. Kempner claimed substantial reduction of hypertension from prolonged treatment with a 2 000 calorie diet consisting of rice, fruit juices and sugar with vitamin and iron supplements. Substantial lowering of blood pressure may be expected in 70 per cent. of cases by virtue of the low sodium content (85 mg.). The Kempner diet cannot be tolerated for more than a month or two because of its insipidity. Whatever type of diet is used, the sodium chloride content should not exceed 0.5 G. daily.

Mental tranquillity and sound sleep may be secured by the exhibition of hypnotics. Phenobarbitone alone (gr. 13 daily) or in combination with theobromine as in Theobromine and Phenobarbitone Tablets B.P.C. 1-4 daily is a popular remedy. Iodides produce symptomatic relief in some cases, but their value is greatest in the rare examples of syphilitic origin. Venesection has a transitory effect, not entirely divorced from the psychological. Vasodilators have little effect on the general level of blood pressure and have been discarded in favour of ganglion blocking agents.

Ganglion blocking agents Paton and Zaunus showed that the methonium halide compounds tetra (C4) penta (C5) and hexa (C6) cause blocking of sympathetic and para sympathetic ganglia. The sympathetic effect is useful in hypertension while the parasympathetic block gives rise to side-effects such as ciliary paralysis dry mouth and skin constipation and urinary retention. C5 and C6 may be used orally or parenterally but the oral route is uncertain and the dose must be five to ten times larger than the injection one. This approximates closely the toxic level. bromism is an added danger which can be averted by using tartrate or chloride. Oral dosage should begin with 250 mg daily and be gradually increased until a moderate reduction in pressure is registered the average requirements being 500 mg four hourly. As with all antihypertensive administration the patient should be up and about during stabilisation so that overshooting and severe postural hypotension may be avoided (cerebral or coronary thrombosis may be precipitated). Great caution must be observed in treating patients with renal defect as serious accumulation may occur. Other disturbing side-effects are bowel upset ranging from constipation to paralytic ileus and retention of urine. Aperients like senna and cascara are more useful than magnesia or liquid paraffin in this connection.

Hexamethonium subcutaneously or intramuscularly is useful for the symptomatic therapy of hypertension. Individual response varies and it is well to observe the effect of a small dose say 15 mg of Hexamethonium Tartrate Injection B.P. The amount may then be increased to 15-20 mg three daily and if this proves uneventful further increments are given until 150-200 mg daily is reached. Continuous normotension is not the aim but a reasonable sustained fall with normal lability. Tolerance of these drugs complicates therapy by either route but it diminishes after one or two months treatment dosage must be reviewed frequently.

Best results are obtainable in cases of severe hypertension without gross vascular or renal change. Lessening of symptoms such as headache vertigo insomnia and dyspnoea may be expected in suitable cases. The treatment is often successful

in aborting encephalopathic episodes and is valuable in left ventricular failure. It will control the secondary hypertension which often arises after an apparently successful sympathectomy but unless care is exercised in dosage it will accentuate postural hypotension.

Pentaptyridinium pentolinium (Ansolysen M & B) has a potency five fold that of hexamethonium bromide and the effect is more prolonged intolerance is less marked. Oral dosage (unsatisfactory) is in the region of 20 mg. (test) after which 300 mg is given daily and increased by 20 mg daily until 1400 mg is reached. Initial subcutaneous dosage is 3.5 mg and this may be gradually increased to 30-60 mg daily. The evening dosage should be double that given in the morning.

In contrast to the ganglion blocking agents is the group with humoral antipressor action. Hydergine Sandoz is a mixture of methanesulphonates of ergot alkaloids which has a peripheral adreno-sympatholytic effect. 1-hydrazinophthalazine, hydralazine (Apresoline Ciba) inactivates several pressor substances e.g. pherentasin, angiotonin while increasing blood volume, cardiac output and most importantly renal flow. It is given in mouth dosage of 100-800 mg daily by divided fractions. It is useful in the same types of progressive benign hypertension as hexamethonium in the post sympathectomy hypertension and in malignant hypertension. It has been given in combination with reserpine, an alkaloid from *Rauwolfia serpentina* which has a similar but milder hypotensive action. A syndrome similar to systemic lupus erythematosus has occasionally been attributed to this drug.

Rauwolfia alkaloids exert a mild antitensive action and control mental excitement and agitation. Occasionally a depressive psychosis may be induced and an antidiuretic effect occasionally leads to fluid retention and cardiac embarrassment. The dose of reserpine (Serpasil Ciba) is 0.5 mg orally daily gradually increasing to 3 mg. Useful in combination with mecamylamine or pempidine as it reduces the individual requirement appreciably.

Mecamylamine (Inversine Merck Sharp & Dohme) acts by sympathetic ganglion block but being a secondary amine

intestinal absorption is satisfactory. This drug is an effective hypotensive with more prolonged effect than parenteral pentolinum and tolerance is unusual. Initial dosage 2.5 mg morning and evening gradually increased as necessary up to 100 mg daily. Side effects particularly gastro intestinal may be prominent they resemble those described under hexa methonium and are treated by laxatives and salines.

Pempidine tartrate (Perculyse: M & B Tenormal ICI) is the most reliable and predictable antihypertensive available. Dosage must be cautious initially 2.5-5 mg daily orally slowly increased to 10-40 mg in four divided doses daily. Side effects apart from dry mouth and constipation are rare and tolerance is not a troublesome feature. Renal defect necessitates very small dosage. Pyloric stenosis and alkaline therapy are dangerous (the drug is best excreted in acid urine). Reserpine (under 0.5 mg daily) and chlorothiazide (up to 1 G daily) potentiate pempidine and with either smaller doses of hypotensive suffice (Hypokalaemia must be avoided).

Antidotes Methoxamine hydrochloride (Vasoxin B.W.) 3-10 mg intramuscularly or intravenously is a useful antidote to overdose with hypotensive drugs. Parasympathomimetic drugs will diminish the effects of parasympathetic block for blurring of vision—essence eyedrops or spectacles with tinted corrective lenses for dry mouth—gr 1/32 pilocarpine in water before meals for abdominal distention urinary retention impotence—15 mg neostigmine subcutaneously.

Surgical treatment Smithwick's extensive dorso-lumbar sympathectomy produces appreciable lowering of blood pressure levels. The operative mortality is not negligible and at best the hypotensive effect wears off in one to three years. Smithwick's experience suggested that groups with ocular cerebral cardiac or renal change where the diastolic blood pressure is not above 140 and without extensive renal damage show a much better survival rate than medically treated controls. The operation will sometimes prolong life and preserve useful vision in progressive malignant hypertension.

The scope of sympathectomy has narrowed with the advent of reliable hypotensive agents but the operation has a place in cases intolerant of dietetic and drug routines and post-operatively the patient will be more sensitive to hypotensives. Thorn submitted a small series of hypertensives with advanced cardiovascular complications to total adrenalectomy. Blood pressure reduction was not universal in the survivors but symptomatic improvement resulted in all. In other clinics the results of this operation have been mixed. Replacement therapy by cortisone is necessary.

Hypertensive encephalopathy. Episodes consisting of severe headache, vomiting, visual disturbances, convulsions and transient pareses may complicate simple or malignant hypertension. They must be distinguished from uremia, cerebral vascular accident and cerebral neoplasm. The immediate prognosis is usually good and they should be treated by venesection (up to 20 oz), withdrawal of cerebrospinal fluid by lumbar puncture and parenteral pentolinum. Hypertonic solutions e.g. 50 per cent glucose 50 ml intravenously are useful in emergency. Morphine is indicated if the convulsive state persists. Severe hypertensive crises respond best to hypothermia (see p. 304).

Hypertension with renal involvement requires treatment as for chronic nephritis.

Coronary Occlusion

Early diagnosis is important. Many cases show a warning phase and if such herald symptoms as unaccustomed breathlessness on exertion, substernal discomfort or unusual dyspepsia on exertion after meals are correctly interpreted the outlook is greatly improved.

In the attack two urgent priorities present themselves: absolute rest and relief of pain. The patient should be put to bed with a minimum of effort on his part and a subcutaneous injection of morphine given ($\text{gr } \frac{1}{2}$ to $\frac{1}{4}$) and repeated if relief is not obtained within the hour. If devastating pain and severe shock are present morphine $\text{gr } \frac{1}{2}$ should be given intravenously at the onset. Other suitable anodynes are methadone 20 mg intravenously and Papaveretum. Injection B.P.C. 1 ml intramuscularly. Oxygen inhalations in

concentration of 90-100 per cent by B.L. II or other efficient mask or tent are used routinely during the first eight to twelve hours in some clinics for relief of myocardial hypoxia. Vasodilators such as amyl nitrite by inhalation aminophylline (0.25-0.5 G intravenously) and papaverine (gr 2-6 intravenously) are often ordered but their value is a matter of speculation and the use of amyl nitrite is not without risk.

Persistent primary shock is associated with a mortality of about 80 per cent. Some cases respond to pressor amines with distinct improvement in outlook. Secondary shock is usually accompanied by cardiac failure and digitalisation is required in addition to vasopressor therapy. Results in this group are in general disappointing.

L noradrenaline (1 arterenol Levophed Bayer Products) exhibits a profound vasoconstrictor action and is safer against hypertension than adrenaline in that the cardiac output is not increased bradycardia rather than tachycardia is the rule and the cerebral stimulant effect is slight. The contents of one 4 mg ampoule are added to one litre of glucose saline blood or plasma according to whether dehydration anaemia or pure peripheral vascular collapse predominates. Each ml of transfusion fluid contains 4 μ g of L noradrenaline and the intravenous drip is adjusted to 20-30 drops per minute in order to maintain the blood pressure above 100 mm Hg (the initial requirement is usually about 2 ml per minute). In a successful case the blood pressure tends to stabilise around this figure after twenty four to forty-eight hours when the L noradrenaline drip may be gradually dispensed with. Regular blood pressure observations are essential during treatment and careful watch must be kept for signs of venous overload (pulmonary basal moisture venous distension). Venospasm sometimes interferes with drip flow this may be lessened by heating the limb by hot packs or electric pad.

Incominence may be combated by a barbiturate and patients who are mentally or physically restless benefit from a tranquiliser. We have found the phenobarbitone-promethazine-chlorpromazine cocktail (p. 11) most useful after the second or third day.

Food may be neglected for twenty four hours after this a light varied diet is allowed. If the patient is overweight the intake must be adjusted accordingly. Smoking should be given up during the stage of bed rest. After forty-eight hours the bowels may be moved by liquid paraffin and magnesia but harsh aperients are to be avoided. By the fourth day if all goes well he may be allowed to rise to a commode placed beside his bed. Exercises of the limb and respiratory muscles should be practised daily to discourage phlebothrombosis and by the eighth day a patient who presents no untoward signs or symptoms may be allowed to sit in a chair by the bedside for five minutes and the time gradually extended.

In cases of average severity rest should be maintained for three weeks in order to permit the establishment of collateral circulation to the infarct area. Mental tranquility is important but boredom is to be shunned. The invalid may be allowed to sit up in bed for washing and for meals after the second week. If free from symptoms he should devote the fourth week to sitting quietly in a comfortable chair to moving around the bedroom and visiting the bathroom if stair-climbing is not involved. By the end of the seventh week the average patient is up for about eight hours has the freedom of his house (including a minimum of stair-climbing) and can take short walks in the garden or on level roads without discomfort. By the end of the twelfth week resumption of a modified business or professional routine as a half timer is usually safe. Dyspnoea and substernal discomfort at any stage are indications for temporary restriction of physical activity.

Except in young subjects return to occupations involving much physical or mental strain is undesirable. The intelligent patient will seek a suitable compromise for six or twelve months after which time his cardiac limitations will be assessable. The liability to recurrence should be explained to the relatives.

Anticoagulant therapy. Heparin and the coumarins are used to prevent extension or dissemination of intravascular thrombi and there is evidence (although not undisputed) that the risk of recurrent infarction is thus lessened. Anticoagulant therapy is more essential in the poor

risk cases than in mild cases in which the mortality is estimated as low as 1 per cent. Many clinicians reserve anticoagulants for elderly patients and those with previous history of coronary accident persistent pain or shock major arrhythmias gallop rhythm antecedent hypertension with enlarged heart obesity diabetes or other debilitating illness it is in these that the risk is greatest. Patients whose prothrombin activity has been adequately controlled may safely be allowed out of bed sooner than those not so treated. It is important to continue anticoagulant therapy for at least two weeks after resumption of modified activity.

Heparin acts on the clotting mechanism present in the circulatory blood within thirty minutes and it is used initially to cover the twelve to thirty six hour latent period of oral anticoagulants. A solution containing 5 000 i.u. (62 mg.) per ml. is convenient for intravenous use. 10 000 i.u. is given six hourly during the first twenty four hours and thrice on the second day. The clotting time should be maintained at fifteen to twenty minutes. Heparin solutions of 25 000 i.u. per ml. may be used in dosage of 15 000 i.u. twelve hourly by intramuscular injection for cases where intravenous dosage is impracticable. They prolong the clotting time satisfactorily but extensive haematoma formation may follow. This risk can be minimised by placing the solution deeply in the muscle mass with a fine gauge needle and by applying pressure for a few minutes afterwards. This route is not recommended for frail elderly subjects. Dextran sulphate (Dexulate Glaxo) intravenously is reported equally effective and more prolonged in action.

The oral anticoagulants act by depressing hepatic prothrombin formation and daily or alternate daily prothrombin activity estimations are essential for safe therapy. 300 mg. of dicoumarol is given orally on the first day and 200 mg. on the second and third days. Usually the drug is administered twice daily the dose being adjusted in accordance with the day's prothrombin figure. The aim of treatment is to reduce prothrombin activity to 20 per cent. of normal if allowed to fall below 10 per cent. haemorrhages are liable to occur. The maintenance dosage varies from 50 to 150 mg.

daily and treatment should be kept up for four to eight weeks or in certain cases for months or years. Tromexan Geigy an oxycoumarinyl derivative has displaced dicoumarol on account of its shorter latent period and less cumulative effect. Dosage initial 900-1 200 mg followed by 300-600 mg daily. Warfarin sodium (Marevan Evans) is said to be the most satisfactory anticoagulant. Daily dose 30-70 mg.

Phenindione (Dindevan Evans) is a popular synthetic anticoagulant. Potency is intermediate, cumulation is slight and individual requirements tend to be stable. Administration and control are as for the coumarins. Dosage is 200 mg. in the first twenty-four hours and 100 mg. in the second maintenance is in the region of 25-75 mg. daily.

Anticoagulant overdosage if due to heparin can be corrected by one or more intravenous injections of 2.5 ml. of 1 per cent solution of protamine sulphate. Transfusion of fresh whole blood is necessary if bleeding is severe. Manifestations of coumarin and phenindione toxicity e.g. hæmaturia and purpura are controlled by phytonadione (Konakion Roche) 10 mg intramuscularly or 1-2 10 mg capsules in milk. Severe bleeding is met by transfusion. Contra-indications to anticoagulant measures are hæmorrhagic diatheses, ulcerative lesions e.g. peptic ulcer, unhealed wounds, poor renal or hepatic function, subacute bacterial endocarditis and advanced pregnancy, some would add senility to this list.

Digitalis is indicated in the presence of congestive failure but it should be used with circumspection on account of the danger of provoking ventricular fibrillation. Quinidine sulphate (gr. 6 two hourly for srt doses) or procainamide (250-500 mg orally three hourly) should be given for auricular fibrillation or paroxysmal tachycardia complicating coronary occlusion. Some physicians employ these prophylactically in cases showing frequent premature ventricular contractions. Conduction defects tend to lessen spontaneously as healing progresses. For ventricular tachycardia procainamide solution 2-3 ml intravenously slowly is the most effective remedy.

For left ventricular failure aminophylline 0.5 G in 50 ml of 50 per cent glucose given slowly into a vein will help

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to limit pulmonary edema. Aminophylline should be continued in oral dosage (0.75 G. daily). Oxygen inhalations are of value. (For management of cardiac arrhythmias see page 210.)

Angina Pectoris

The general routine described for arteriosclerosis and hypertension should be followed. Exertion should when possible stop short of provoking pain and factors predisposing to attack such as flatulence tobacco cold and strong winds should be avoided. Worry emotion and excitement are detrimental. Syphilis if present should be cautiously treated on the lines suggested for cardiovascular manifestations.

Vasodilator such as papaverine aminophylline sodium nitrite and glyceryl trinitrate are sometimes of assistance in lessening the frequency of attack. Combined treatment with phenobarbitone gr 23 daily and Glyceryl Trinitrate Tablets B.P. gr $\frac{1}{15}$ sublingually every four hours gives best results. Trinitransine trinitrate (Practitrans Schering) is given in oral dosage of 3.8 mg. daily. With a background of this drug less frequent recourse to nitroglycerin is necessary. Rauwolfia preparations are useful as background therapy also particularly in subjects prone to excitement and hypertension. Penterythritol tetranitrate exerts a very indifferent vasodilator action. Sublingual nitroglycerin remains the most effective treatment of the anginal attack and it should be used promptly at earliest warning.

Radiiodine therapy has been suggested for intractable angina. It benefits the sufferer by lessening circulatory demands and the physiological responses to adrenaline. Nicotinic acid and testosterone propionate are occasionally used in effort anæmia following cardiac infarction. Status arginosus should have treatment as detailed for coronary thrombosis.

Where frequent anginal paroxysms make the patient's life a burden one or other of the surgical measures designed to lessen cardiac ischæmia may be considered. They are not conspicuously successful.

To lessen pain and coronary spasm

Anterior rhizotomy in which the upper four or five thoracic nerve roots are divided on both sides

Paravertebral block preferably by procaine This is the most popular resource

Cervicothoracic ganglionectomy in which the stellate and T1-5 sympathetic ganglia are removed on one or both sides

To improve the coronary circulation

Implantation of the internal mammary artery into the myocardium

Partial occlusion of the coronary sinus by ligature alone or with formation of an anastomotic channel between the aorta and coronary sinus

Insertion of talc powder into the pericardial sac which causes vascular adhesions

Aneurysm

The principles enunciated for the management of arteriosclerosis hold good Rest is of prime importance and the diet should be light and dry Syphilitic aneurysm should be treated by iodides bismuth and penicillin Symptomatic measures for the relief of pain and hypertension are usually necessary

The scope of vascular surgery has widened during the past decade The present tendency is to excise saccular aortic aneurysms Excision of the dilated segment with replacement by aortic homograft or plastic tissue has proved successful Dissecting aortic aneurysms can be dealt with if in the ascending arch by providing a re-entry to the aortic lumen if situated in the descending arch by excision of the false entry segment or of the intima Flatform abdominal aortic aneurysms may be reinforced by a plastic wrap around Peripneural aneurysms present fewer problems than aortic and the results of surgical removal are gratifying

Peripheral Arterial Obstruction

This may be caused by embolism or thrombosis In the latter case the obstructed vessel has previously undergone

degenerative change. Obstruction in an arteriosclerotic subject results in gangrene of a distal portion of the limb. Embolectomy is feasible if the case is seen early; later amputation is usually necessary.

Interim treatment consists of keeping the ischaemic portion of the limb cool by exposure to the air. The rest of the body should be maintained in an air temperature of 110° F by electric cradles. The skin of the affected limb must be kept surgically clean by the use of spirit and antiseptic dusting powders. Tolazoline hydrochloride (Priscol, Ciba) and pyridylcarbinol (Roneol, Roche) have been used intravenously for their vasodilator action with doubtful benefit. Sympathetic block with procaine will improve the collateral circulation and anticoagulant therapy is of value.

Localized intra-arterial block is amenable to surgical attack. For example, thrombosis of the aortic bifurcation (Leriche's syndrome) may be relieved by thrombo-endarterectomy, segmental resection with insertion of homograft or provision of a by-pass according to extent and distribution of the endarteritis.

Intermittent Claudication

A troublesome manifestation of endarteritis and arising from muscular hypoxia induced by exercise. It adds a distressing limitation to the patient's activities. Tocopherol and tolazoline and other vasodilators are of no value. Lumbar ganglionectomy in patients under sixty years who show good response to vasomotor tests may relieve cold feet but not the claudication pain. Extensive ulceration, gangrene or myocardial defect are contra-indications. Arteriography frequently demonstrates a localized occlusion of the popliteal artery; here a graft arranged to surmount the block is curative. Patients who are unsuitable for sympathectomy on account of age or general condition eventually gain relief by amputation.

Tenotomy of the tendo achilles will relieve pain of gastrocnemius or soleus origin. Pain in the anterior tibial peroneal group is lessened by section of the external popliteal nerve but these operations have obvious disadvantages.

Thrombo-angitis Obliterans Buerger's Disease

Tobacco is undoubtedly harmful and should be given up. Alcohol is of some therapeutic service on account of its vasodilator action. A month's rest in bed is advisable at the outset especially in the presence of thrombophlebitis. Loose warm clothing should be worn and heat provided by the use of electric pads or cradles. The Buerger method of passive vascular exercise may be given trial.

With the patient lying supine the affected limb is elevated to an angle of 60° to 90° for one-half to three minutes until blanching appears. It is next allowed to hang down over the bed edge for two to five minutes until hyperæmia occurs. The limb is then placed horizontally and heat applied by means of hot water bottles or an electric pad. This sequence is repeated for an hour and several sessions are gone through daily.

The rocking bed treatment is favoured in some clinics. Ulcers must be dealt with surgically.

Lumbar sympathectomy is of value in the distal types of thrombo-angitis particularly those which show very slow progression. Operation is contra-indicated in severe arterial insufficiency and gangrene.

Polyarteritis Nodosa

A necrotising pan arteritis with collagenous degeneration involving the arterial system generally. Symptom patterns are complex and the disease often fatal. Treatment is directed to maintenance of nutrition which is something of a problem in view of the protracted and debilitating nature of the illness. Liberal diet, vitamin supplements, blood transfusion, fresh air and bed rest are essential and symptomatic indications should be met as they arise. Pyrexia is usually unresponsive but penicillin or chlortetracycline is worthy of trial. Asthma, polyneuritis, anaemia, renal, hepatic and cardiac involvement are treated routinely. Cortisone is of considerable value in some cases although renal lesions are resistant.

Temporal Arteritis

Characterised by visible inflammatory changes in the temporal arteries but many other arteries are involved. Pyrexia headache visual defect and mental change are common. Biopsy of the affected temporal artery or periauricular sympathectomy have given relief. Vitamin B concentrates chlor-tracycline and cortisone have also been credited with cures.

Raynaud's Syndrome

May be symptomatic of various conditions such as syphilis lupus erythematosus thrombo-angitis obliterans cervical rib and myelomatosis. It is an occupational risk in pianists typists and those who handle vibratory tools. Raynaud's disease occurs most frequently in young women, has no aetiology other than poor circulation and is often inherited. It is an expression of reaction to cold and in mild form is the dead fingers of sea bathing addicts. A warm climate is ideal. Cigarette smoking should be given up. A liberal nourishing diet with full allowance of fats and vitamin supplement is beneficial. Drugs have very limited value in this condition but tolazoline hydrochloride 4 tablets daily may be tried in mild cases. β -pyridylcarbazole (Ronicol, Roche) a nicotinic acid derivative has a similar but more sustained dilator action on the arterioles. Oral dosage 100-200 mg daily. Cortisone has been used with some success in sclerodermatous cases.

Exposure and chilling of the extremities should be avoided. Warm woollen garments loose mitten fur lined gauntlet gloves without separate finger compartments two pairs of stockings (one of wool) and fleece or fur lined boots are desirable. Irritation and trauma of the extremities must be avoided since trophic alteration is slow to heal.

Sympathectomy is usually reserved for the disease rather than the syndrome and it raises the threshold for cold in cases showing severe and progressive vasospasm, scleroderma or painful superficial skin ulceration. The extent of the sympathectomy varies with the severity of the scleroderma. If the face neck and arms are affected T1-5 roots are interrupted.

Peripheral Venous Thrombosis

This condition occurs in debilitating states *e.g.* pneumonia the post-operative state and in elderly bed fast subjects. Prevention is on the lines mentioned in page 269. For treatment complete bed rest with immobilisation of the affected leg by sandbags and cradle together with a soothing local application *e.g.* glycerin of ichthyol.

Anticoagulant therapy is desirable in extensive cases until moderate activity can be regained (p. 241). Cortisone, phenyl butazone and para aminosalicylic acid have been recommended for the active stage and they certainly relieve pain. Passive movements should begin when local pain and oedema have subsided and the patient encouraged to walk (with bandages on both legs) to prevent further incidents. The use of a donkey or pillow under the legs or slouching in an easy chair should be avoided both for prevention and cure as they impede venous return from the lower limbs.

Thrombophlebitis migrans. In addition to treatment of each thrombotic incident a prolonged course of anticoagulants should be given. Ligation of the veins and occasionally of the inferior vena cava may be necessary.

Congenital Heart Lesions

Minor abnormalities such as small septal defects and cusp lesions give rise to no symptoms unless infection supervenes. Cases with pulmonary obstruction and veno-arterial shunt suffer from cyanosis and dyspnoea which are accentuated by muscular effort. Aortic coarctation produces a compensatory arterial hypertension and the proximal aorta may become the seat of degenerative changes.

Treatment, other than surgical is directed to limiting the child's activities in proportion to the circulatory defect. Later he becomes most expert at doing this for himself. Upper respiratory infections, rheumatism and septic lesions in general have dangerous potentialities in these cases and every care must be taken to prevent their occurrence.

The surgical treatment of congenital cardiac anomalies has of late made phenomenal progress.

Patent ductus arteriosus Ligature and preferably division of the ductus lessens the substantial risk of infective endocarditis. The elective operation introduced by Gross should be done at about the age of four years although good results (with higher operative risk) attend its performance even in adult life. If operated on before the age of twelve years growth and development approximate normal. For established infective endocarditis adequate antibiotic therapy should be instituted and the ductus ligatured as soon as the blood stream has been cleared of organisms. Cases showing permanently reversed shunt are unsuitable for surgery.

Coarctation of the aorta The adult type of deformity if distal to the origin of the left subclavian artery is corrected by excision with end-to-end suture of the aorta. The more extensive infantile type of deformity is treated by excision of the constricted portion of the aorta and anastomosis between the left subclavian artery and the side of the aorta distal to its division. Excision of an extensive constriction with insertion of a homograft has been successfully accomplished. Other aortic anomalies such as double arch and long nital aneurysm of the descending aorta have been remedied by operation.

Congenital pulmonary stenosis and Fallot's tetralogy The provision of an anastomosis between a subclavian or innominate artery or aorta and pulmonary artery will improve the pulmonary circulation and correct cyanosis. Operation should not be done before the age of eighteen months; between five and ten years is the best time. In older patients the vascular structures are less resilient and technical difficulties of the operation are increased. Pulmonary systemic shunts of the Blalock Potts type have a mortality of 10 per cent but afford symptomatic relief in about 80 per cent of cases. Brock has attacked the problem fundamentally and his valvotomy technique gives excellent results in subjects with isolated valvular stenosis. He has also devised a resection operation for infundibular stenosis but the ventricular septal defect should ideally be repaired at the same time. These operations are rapidly becoming more effective due to improved technique and in a given case the decision as to whether they are likely to give better results

than anastomotic procedures is not always easy. Some cases of Fallot's tetralogy are unsuitable for valvotomy but there remains a large proportion in whom the question of shunt versus valvotomy propounds itself. The latter is more physiological and removes an anomaly whereas the anastomotic operation adds one.

Septal defects. Surgical attack on these has been hindered by the difficulty of working blindly in a bloody field. Bigler and his colleagues found that by cooling the body metabolic processes could be damped down sufficiently to allow interruption of the cardiac pump for a short period without harm. Good progress is being made with the extra-cardiac circulatory pump which will solve the problem of a dry operative field. Meanwhile Gross has closed small interatrial defects by suture and sizable defects by suturing a nylon patch over the defect. His approach is through a funnel-shaped rubber well which is sutured to the left auricle before opening that chamber. The well fills with blood which is heparinised and this temporary loss of blood from circulation is compensated for by transfusion.

Cardiac Neurosis

A diversity of symptom patterns all loosely mimicking true cardiac lesions are produced by imaginative patients who labour under psychological difficulties. There is often a familial or environmental background conducive to neurosis. Many cardiac neuroses originate in uninformed or ill-considered medical advice. The diagnosis of a tired, strained or weak heart, the prohibition of games to a schoolboy in the absence of proven cardiac defect or the magnification of minor increases or decreases of blood pressure into pathological entities may sow the seeds of needless invalidism.

Effort syndrome is the commonest form of cardiac neurosis and it burgeons in time of war. Conscripts from sedentary occupations are forced into the discipline of a herd existence. The strenuous training of a soldier in war must of necessity be imperfectly graded at times. Finally he is thrust into a bloody business for which he has no stomach. These factors operating on an inadequate personality may call

forth protective disability in the guise of chronic headache intractable dyspepsia or cardiac discomfort

Treatment is difficult and not conspicuously successful. Complete physical examination should be made at the outset and negative findings may reassure the sufferer. The psychophysiology of the patient's symptoms should be explained to him and abreaction technique is often effective in cases arising out of battle stress or catastrophic accidents. Carefully graded physical re-education at the hands of capable and understanding instructors will cure a proportion of cases. Psychiatric analysis of the patient's environmental maladjustments with guidance for their resolution is helpful. Recruitment should be allotted to various arms of the service on results of psychiatric assessment at entry. A system of interview selection of entrants to industry has proved mutually beneficial to management and labour force.

CHAPTER XIV

DISEASES OF THE RESPIRATORY SYSTEM

Acute Catarrhal Rhinitis

Treatment of the common cold is largely empirical. In the invasive stage a hot bath, an aperient, a diaphoretic and twenty four hours rest in bed will often cure the complaint. For established infections confinement to bed in an even temperature for two or three days is the best remedy. Febrile symptoms should be treated by an alkaline diaphoretic mixture or by a few doses of aspirin and Dover's powder. Inhalations of steam medicated with menthol or friars balsam help to relieve nasal obstruction caused by mucosal turgidity. Decongestants such as ephedrine 0.5 per cent in normal saline may be sprayed or instilled into the naso-pharynx three or four times daily. Nasal douches sometimes spread infection to the accessory sinuses or Eustachian tubes and their use is to be discouraged.

Sinus block is a frequent concomitant of nasal infections and causes characteristic pain and sense of fullness. If unimproved by the use of Penicillin and Ephedrine Nasal Drops B.N.F. a pledget of cotton wool containing 5 per cent cocaine may be inserted in contact with the middle turbinate for fifteen minutes. Frank sinus infection requires surgical treatment usually replacement of exudate by penicillin solution.

Premature return to everyday duties should be frowned upon.

Chronic or recurrent colds raise the presumption of nasopharyngeal or pulmonary disease and appropriate investigations are called for.

Acute Tonsillitis

The patient should remain in bed in a comfortably warm room until the temperature has fallen to normal. A light

pulveraceous diet consisting of gruel, jellies, milk foods, ice cream, sweetened fruit juices and barley water ■ satisfactory. The possibility of diphtheria should be excluded by examination of throat swabs, but the question of administration of diphtheria antitoxin must be decided on clinical grounds without waiting for culture results. Other conditions in which sore throat is common, such as scarlatina, glandular fever and syphilis must be borne in mind.

Tonsillitis due to acute streptococcal infection responds to sulphonamide therapy, and penicillin ■ even more rapidly effective. Penicillin is the best remedy for infections with Vincent's organisms. Two or three doses of 200 000 units or 12 ml of procaine penicillin intramuscularly daily will usually control acute tonsillitis within forty-eight hours.

Patients should not be entrusted with sulphonamide or antibiotic preparations for continued local use, e.g. lozenges and nasal drops, as sensitisation may follow their indiscriminate employment.

Cervical adenitis. Quickly relieved by effective antibiotic therapy. Kaolin poultices are useful. Abscess formation requires surgical treatment.

Peritonsillar abscess. Energetic penicillin therapy will abort the condition if commenced early. The abscess involves the soft palate and usually points in the supratonsillar fossa between the fifth and ninth days. The patient should sit upright or recline on the affected side and the head is steadied by an assistant. A head light is essential. A stout bladed bistoury is sterilised and wrapped so that only half an inch of the blade at the point is free. The tongue ■ protected by a tongue depressor and a downward stabbing incision about $\frac{1}{2}$ inch long made over the point of maximum bulging, usually at the intersection of two lines, one drawn horizontally through the base of the uvula and the other at right angles to this and touching the anterior faucial pillar (keep away from the base of the uvula and the upper pole of the tonsil). Further treatment consists of frequent gargles of hot saline. If the abscess has ruptured spontaneously drainage should be facilitated by inserting the closed points of a sinus forceps and opening the blades slightly. A general anaesthetic is unnecessary except for children.

Chronic or recurrent tonsillitis and quinsy are indications for tonsillectomy during a quiescent interval

Hay fever

The unpleasant manifestations of this condition may show a strictly seasonal incidence limited to the pollination period of the plant responsible. A second type is the perennial vasomotor rhinitis in which more general sensitivity exists to dusts and animal dandruff as well as to pollen.

The allergic nose rarely benefits from surgical interference but gross abnormalities should be corrected. Skin sensitivity tests should be done by scratch patch or intradermal methods using pollen and dust extracts which are available from Messrs Bencard Messrs Duncan Flockhart and others. Sometimes a particular pollen can be incriminated from the patient's history but this should be confirmed by skin tests. Grass pollen is the most frequent offender.

Cases of the perennial type often react to a multiplicity of dissimilar substances and non specific immunisation must be tried.

Preparations of group and single allergens in common use are obtainable commercially others can be had to order. Attempts should be made to raise the patient's threshold to attack by a course of fifteen to thirty graduated injections of the offending protein. Best results are obtained by commencing the course in January and using twice weekly intervals in the beginning and weekly intervals with larger doses. If leisurely prophylaxis is impossible the course may be given by daily or alternate daily injections. Dosage should be large but stopping short of dermal nasal or general reaction. A few minims of adrenaline mixed with the early doses will retard absorption and improve tolerance. Larger doses of adrenaline must be given to control sensitivity reactions. Reaction should be met by halving the dose and working up again. Severe reactions respond to prompt administration of ephedrine gr $\frac{1}{4}$ 1 or adrenaline 1 : 1000 solution 5-10 minims hypodermically. Antihistaminics and cortisone are useful for prevention and cure. Local reactions may be disregarded.

Co-seasonal treatment For latecomers already beleaguered

by their particular pollen Freeman's rush inoculation method may be used. The patient should be admitted to hospital and graduated subcutaneous injections given at 1½ hourly intervals by day for two or three days.

Treatment of the attack. Ephedrine gr ½ thrice daily is a useful stand by and should be taken throughout the pollen season. The wearing of tinted spectacles helps to keep the conjunctivæ free of pollen.

Adrenaline is the most efficient drug. If given early in the attack a few minims hypodermically brings prompt relief while Hyperdure Adrenaline and adrenaline in oil will maintain freedom for several days. Sufferers who are averse to self injection may use tablets of isoprenaline 30 mg under the tongue on rising.

A severe attack may be rapidly terminated by cortisone 150-300 mg orally daily reducing to 12½-25 mg daily for maintenance. Deltasteroids one fifth these amounts.

The antihistamine drugs such as diphenhydramine hydrochloride Benadryl P.D. are useful palliatives in hay fever and hay asthma. They sometimes produce a considerable measure of relief particularly in cases where the allergen cannot be identified. They should be given during the period of desensitisation until the latter has progressed sufficiently to limit symptoms. Initial dosage should be small e.g. one capsule or tablet night and morning and in the absence of undesirable toxic effects (drowsiness, nausea, vertigo and syncope) this may gradually be increased four fold. Diphenylpyraline Histyl Spansules S.T. & F. one 5 mg capsule night or morning is effective over many hours in prevention of attacks.

Local applications

Hydrocortisone as snuff or nasal drops (e.g. Cortibiotic Roussel) is by far the most satisfactory.

Ephedrine 0.5 per cent in normal saline

For instillation into the nostrils and eyes on rising.

Laryngitis

Acute. The sufferer should remain in a well ventilated but warm room the voice is rested and smoking forbidden.

should receive attention otherwise treatment of the bronchitis is likely to fail Chronic bronchitis of any severity is irreversible and often coexists with other pulmonary diseases such as emphysema fibroid tuberculosis bronchiectasis and pneumoconiosis and diagnosis ought to be considered provisional until the possibility of a more serious pulmonary lesion has been excluded

A dry equable climate is most suitable Young patients do well at Alpine resorts where pure dry air and a maximum of sunshine are available but elderly patients with long-standing bronchitis and myocardial change respond poorly to high altitudes

The sufferer should spend as much time as possible out of doors when the weather is mild Deep breathing and setting up exercises are encouraged and mouth breathing and slouching postures condemned postural drainage is useful where sputum is profuse Tobacco and alcohol should be forbidden Undernourished patients are given liberal diet with full allowances of protein and fat obesity increases dyspnoea and stout subjects may with advantage undergo reduction treatment

Drugs Expectorants rarely live up to their reputation but the following may be tried

A warm saline draught on waking (see p 257)

Ammonia and Ipecacuanha Mixture BPC may be reinforced by a few grains of potassium iodide

A drachm dose of sedative linctus (Codeine Linctus BPC Squill Opiate Linctus BPC) on retiring will suppress cough

Antispasmodic remedies are of value where an element of bronchial spasm exists Lobelia and Stramonium Compound Mixture BPC or one containing potassium iodide gr 2 ephedrine hydrochloride gr $\frac{1}{2}$ tincture of belladonna 7 minims and ethereal tincture of lobelia 10 minims may be tried

Chronic bronchial infection is little responsive to chemotherapy but exacerbations are frequent during the winter months usually caused by upper respiratory infections

These should be promptly and efficiently treated by confinement to house or bed and exhibition of a suitable antibiotic. Penicillin, streptomycin and erythromycin are valuable in many cases but for some a short burst of a tetracycline or chloramphenicol is more effective. Continuous therapy with broad spectrum antibiotics throughout the winter months has given good results with little in the way of side-effects (acute and severe respiratory infective incidents 10 G chloramphenicol over five days A. H. Iranzadis *et al.* 1957; advanced purulent bronchitis oxytetracycline or tetracycline 0.5-1.5 G daily throughout the winter J. R. May and N. C. Oswald 1956).

Inhalation therapy. Penicillin and streptomycin aerosols are now rarely used as their good effect is short lived. Detergent mists (Aikvaire, Bayer) are useful in liquefying tenacious sputum. They may be combined with deep breathing, postural drainage and cough routines.

Emphysema

Usually coexists with chronic bronchitis and much of the treatment outlined above is applicable. Occupations involving exposure to expiratory stress, e.g. glass blowing and those demanding strenuous physical exertion or exposure to the elements should be abandoned. Breathing exercises designed to deflate the chest and improve the abdominal musculature are of some value in early cases. Routines designed to secure free movement of the diaphragm and lower ribs should be practised. In more extensive cases an artificial pneumopentothorax will assist expiratory ascent of the diaphragm. For advanced cases expectorants and antispasmodics are helpful. Nocturnal dyspnoea causes apprehensiveness and loss of sleep for which a combination of ephedrine, aminophylline and phenobarbitone should be prescribed. Franol tablets, Bayer, are useful for this purpose. If bronchial spasm is prominent temporary relief follows inhalation of Isoprenaline Sulphate Compound Spray B.P.C. Myocardial weakness calls for rest in bed, venesection, digitalis and aminophylline. Oxygen inhalations are of some value in treatment of cor pulmonale. (See p. 249.)

Pneumonia

Lobar pneumonia A bright well ventilated sick room should be chosen and the air temperature maintained at 65° F. A single bed with a firm mattress facilitates nursing. Absolute rest must be enjoined during the pyrexial stage afterwards in the absence of complications the patient may be allowed to rise to the commode. Diet should be liquid or semisolid in the early stages. Fruit drinks sweetened with sugar or syrup, fruit jellies, milk and its modifications, soups, bread, butter and weak tea are all acceptable. Bowel action may be ignored for the first few days of illness unless discomfort arises when an oil enema or biscodeyl (Dulcolax) suppository may be used.

A precise bacteriological diagnosis is desirable and may be obtained by culture of blood, sputum and nasopharyngeal swabs. Chemotherapy should not be delayed pending the results of these examinations.

Drugs The majority of organisms responsible for lobar pneumonia are sensitive to sulphonamides and this therapy is often indicated on grounds of expediency but if a satisfactory response is not obtained within twenty-four hours penicillin should be given as well. Sulphadiazine and sulphadimidine are two of many suitable preparations. For a moderate to severe case 3 G. should be given initially then 2 G. in four hours followed by 1 G. four hourly until the temperature has been normal for thirty-six to forty-eight hours. 0.5 G. doses are then given at six to eight hourly intervals for three to four days. A fluid intake of 4-6 pints with sodium bicarbonate 2-4 drachms daily must accompany the sulphonamide dosage.

Penicillin is the therapy of choice for lobar pneumonia and it will usually produce speedy resolution of pneumococcal, streptococcal and staphylococcal infections. 12 mega units of crystalline penicillin daily by six hourly intramuscular injections is the routine for average cases. After defervescence change may be made to twice daily intramuscular injections of 1 ml. of a procaine penicillin and many use this type of penicillin throughout the pyrexial period. Once fever has abated daily injections are sufficient. Oral penicillin V is effective and trouble free (125-250 mg

four hourly) Erythromycin and allied preparations are valuable in cases where penicillin is indicated and probably more so in staphylococcal and diphtheroid pneumonias (1.2 G daily)

Streptomycin is of value in some pneumonias which are inadequately controlled by penicillin and sulphonamides e.g. those due to infection with enterococci *H. influenza* *K. pneumonia* (Friedländer). Estomycin Glaxo is a penicillin ester streptomycin combination and each adult dose phial contains 500 000 units and 1 G respectively. This may be given daily.

The tetracyclines and chloramphenicol have no advantage over the older remedies in pneumococcal infections except in circumstances where injections are impracticable. Their use should be reserved for infections with unusual organisms such as staphylococci klebsiellae haemophilus where specifically indicated by sensitivity tests of sputal flora; also in psittacosis and other virus pneumonias. *Pseudomonas pneumonia* rare in this country responds to polymyxin 1.5 mega units intramuscularly daily in divided dosage.

■ the disease resolves without incident the patient may be allowed up after seven days freedom from fever convalescence should be lengthy and iron fish liver oil and vitamin concentrates are useful.

Symptomatic treatment Pleural pain is often troublesome at the outset and should be met by application of heat in the form of kaolin poultices or an electric pad. Restlessness delirium and insomnia occur in alcoholic and debilitated subjects for sedation paraldehyde 3 drachms in whisky or 3.5 ml. by intramuscular injection is least depressant. Alcohol may be necessary in those who are addicted and it is sometimes a useful soporific in elderly abstainers. Barbiturates such as soluble barbitone gr 10 or quinalbarbitone gr 1½ by mouth may be tried in resistant cases. active delirium is best controlled by morphine or Pethidolphan Roche.

Myocardial weakness calls for intravenous administration of digoxin 0.5 mg. or strophanthin gr ⅙ followed by one digoxin tablet (0.25 mg.) by mouth four hourly for six doses. adequate maintenance therapy should be arranged. Noradrenaline (Levophed Bayer) 2 mg. in 0.5 litre of

physiological saline may be given by intravenous drip for critical circulatory failure. Hydrocortisone hemisuccinate by vein is likewise useful for tiding the seriously ill patient over the crisis (See p. 34.)

Oxygen therapy Oxygen inhalations are of service in the presence of restlessness, cyanosis or cardiac weakness. These are most frequently encountered in young children and elderly subjects. It may be administered simply and efficiently by means of a B.L.B. or other close fitting oronasal mask and a flowmeter and washing bottle should be incorporated in the circuit. By closing the air intake ports a high concentration (up to 100 per cent) can be given. The rate of flow should be about 6 litres per minute and the reservoir bag should distend well with expiration.

Oxygen tents are of two types: the enclosed (*Oxygenaire*) and the open (St. George's pattern). The enclosed types consist of an air tight plastic envelope or canopy which encloses the patient's head and trunk. Light nursing routines can be done through cuffs in the envelope. A CO₂ absorber, dryer and cooler are incorporated in the circuit so that the contained air can be accurately conditioned. Smoking and lights are forbidden near the tent as are electric bell pushes. The open type consists of a funnel of transparent plastic material which fits snugly round the neck. The oxygen enters at the bottom near the mouth where a high concentration is required and waste gases spill over the open top. This tent is cheap and efficient.

Complications Pleural effusion is the commonest and it may become purulent. Serous effusion if small requires no special treatment; larger collections should be aspirated. Purulent effusions must be drawn off daily or every other day and replaced by 250 000 units of penicillin in 15-30 ml of normal saline until the exudate becomes sterile. Parenteral antibiotic therapy based on bacteriological data should also be given. A few empyemata clear up satisfactorily under this régime but surgical drainage and toilet of the pleura are required if the purulent collection is encysted, interlobar, multiloculated or too thick for removal by aspiration. Streptokinase and streptodornase may be injected intra-pleurally to aid liquefaction of fibrin and thick purulent

exudates but they rarely replace surgical treatment which should not be unduly delayed

Decortication is necessary where the lung is bound down by a thick fibrinous pleural exudate. Closed drainage is to be preferred as it encourages pulmonary re-expansion and obviates mediastinal shift. Breathing exercises are of great value in this connection.

Pericarditis, meningitis and arthritis require appropriate treatment.

Bronchopneumonia. Treatment is in general similar to that described above. The condition is often superimposed upon some other illness which will require appropriate treatment.

Primary atypical pneumonia. Probably due to virus infection and unresponsive to sulphonamides and penicillin. Dosage with the broad spectrum antibiotics appears to shorten the course of this disease although its comparative rarity, benign course and difficult diagnosis make evaluation of new lines of treatment somewhat unsatisfactory. Chlor tetracycline is given in divided daily dosage of 1.5 G by mouth until defervescence is complete.

Harvester's lung. A diffuse pneumonia condition caused by inhalation of fungi or disintegration products which abound in poorly saved hay. Occupational incidence is marked, the disease being confined to farm workers and animal fodder storemen. It occasionally leads to pulmonary fibrosis and bronchiectasis. Treatment is by potassium iodide gr 100-200 daily.

Asthma

The patient's history should be reviewed in order to elicit evidence of allergy. If a protein or protein group can be identified as causing the patient should if possible be excluded from contact therewith or desensitised. The influence of emotion in precipitating asthmatic attacks is well known, and psychological factors should be sought for. Expert psychiatric guidance is often helpful particularly in children, where a parental attitude of over anxiety may encourage the child to dramatise his malady. The patient's mode of life may have important bearing on the disease. Exposure to cold, damp and dusty atmospheres is harmful. Irregular meal hours and

unsound dietetic tendencies must be avoided. Abnormalities of gastro-intestinal function should be corrected and a plain nutritious diet given. Where the attacks are frequent and severe temporary resort to a lacto-vegetarian regime may help to break the vicious cycle. Nocturnal asthmatics should not take late evening meals. Carbohydrate metabolism is occasionally defective and a depressed sugar tolerance curve is an indication for dosage with 2 oz. glucose daily. The asthmatic should be encouraged to live as full a life as possible and any tendency to an atmosphere of invalidism dispelled. Recreation in the open air is particularly beneficial.

The influence of dental, tonsillar and sinus infections and of nasal polyposis has been variously estimated but there is no doubt that asthmatic phenomena can be aggravated by their presence. Ritual operations such as turbinate cautery produce only ephemeral benefit.

A complete examination of the chest should be made. Associated conditions such as bronchitis, emphysema and tuberculosis will dictate modifications of treatment. Radiology and bacteriological examination of the nasopharyngeal and bronchial secretions may afford helpful information.

It is often worth while to study the allergic state of young subjects but in long established cases where the spasmodic phenomena have become less clear-cut and an overlay of emphysema and bronchitis complicates the picture pursuit of allergic tendencies is rarely profitable. Using the solutions commercially available for skin testing it is found that about 10 per cent. of asthmatics show definite reaction to a single protein or group of proteins. If the offending protein is a food stuff it should be excluded from the diet; if it is a ubiquitous substance like house dust or horse dandruff an attempt may be made to render the sufferer hyposensitive by a graduated series of subcutaneous injections. Many asthmatics show general sensitivity by reacting to a bewildering assortment of heterogeneous proteins and for these non specific desensitisation should be tried. Mixed Inhalants Solution. Bencard is a preparation of considerable general utility. It is obtainable in combination with pollen extract for use in cases of hay asthma and in strengths suitable for initial and continuation treatment (see p. 254).

Whatever desensitising agent is employed it is imperative to avoid general reactions.

Asthma which is nocturnal in incidence calls for exclusion in turn of the allergen found in bedrooms. A horse hair mattress, feather pillows, eider down quilt and woollen blankets are possible offenders. Some sufferers are sensitive to dusty carpets and as a last resort wall paper may be removed and the walls painted. Asthma is a capricious disease and a change of room or an inconsiderable change of locality may confer freedom.

Physiotherapeutic measures are valuable especially in child asthmatics. Gymnastics, postural and deep breathing exercises and heliotherapy all have merit in individual cases. The exercises are designed to restore thoracic mobility and correct overdistension. Complete expiration with emphasis on the rôle of the diaphragm and abdominal muscles must be taught (See Breathing Exercises G. M. Storey Faber 1958).

Drugs. Iodides and anti spasmodics are useful for routine treatment (Lobelia and Stramonium Compound Mixture B.P.C. or a mixture containing ephedrine hydrochloride gr $\frac{1}{2}$ tincture of belladonna 7 minims and ethereal tincture of lobelia 10 minims three or four times daily). Caffeine Iodide Elixir B.P.C. is a good routine remedy and may be taken in dosage up to 4 drachms daily.

An evening sedative is indicated when the attacks occur at night. A powder containing gr 1 each of ephedrine and phenobarbitone may be given. Ephedrine gr $\frac{1}{2}$ with butobarbitone gr 3 is another useful bed time medication. The antihistamine drugs are of doubtful benefit in spasmodic asthma but are occasionally of value for episodic treatment of child asthmatics and of hay asthma.

Treatment of the attack. REMEDIES WHICH MAY BE SELF ADMINISTERED

1 *Sedatives and antispasmodics by mouth* Quinalbarbitone sodium gr 3 and ephedrine gr 1. Isoprenaline Sulphate Tablets B.P. 0 mg. or Isoprenaline bitartrate Isolevin Wyeth tablets of 15 mg. sublingually.

2 *Antispasmodics by inhalation* Adrenaline 1 : 100 with

glycerin This is combined with other antispasmodics e.g. atropine methyl nitrate sodium nitrate and papaverine in Adrenaline and Atropine Compound Spray B.P.C. and in many proprietary inhalants such as Rybarvin Isoprenaline Sulphate Compound Spray B.P.C. is more effective in some cases and a short inhalation will often terminate the attack. *L* isoprenaline bitartrate Isolevin Wyeth is an effective bronchodilator These may be used in a hand or power operated atomiser

3 *Adrenaline* 1 : 1000 by hypodermic injection The most generally useful remedy 3-5 minims at the beginning of the attack is much more effective than a large dose later

FOR ATTACKS NOT AMENABLE TO THE FOREGOING THE MEDICAL ATTENDANT MAY TRY

Adrenaline 1 : 1000 given by the Hurst method A hypodermic syringe is charged with 20 minims of adrenaline One minim is given subcutaneously and the syringe is then strapped to the patient's skin and the remainder given at the rate of one minim per minute A better result is often obtained if the Hurst dose is divided into four or five subcutaneous injections in various sites Delayed action adrenaline (adrenaline in oil adrenaline mucate Hyperdure adrenaline A & H dose 0.5-1 ml) is useful in some cases

Status asthmaticus If resistant to the foregoing measures often yields to aminophylline 25-0.5 G in 10 ml of saline intravenously Morphine is better omitted in view of its depressant action on the respiratory centre and its suppression of the cough reflex Pethidofan Roche 50-100 mg intramuscularly is a less objectionable antispasmodic. Drug addiction is easily induced in asthmatics so that morphine and its analogues should be avoided whenever possible Sedation is necessary in most cases soluble phenobarbitone gr 3 intramuscularly is safe but a basal dose of bromethol rectally is more certain

Inhalations of oxygen should be given to patients who show respiratory distress A mixture of helium 80 per cent and oxygen 20 per cent is said to give better results than oxygen alone

Antibiotics Asthmatics are notoriously responsive to hospital routine and it is difficult to assess the value of any single item of treatment. In cases where an element of pulmonary, bronchial or nasal sinus infection is present systemic therapy with an appropriate antibiotic is a valuable measure.

ACTH and cortisone In severe asthma and status asthmaticus the administration of these hormones induces a quiet interval of one to four weeks in which the bronchospasm and respiratory difficulty recede. Lost sleep is made up, nutrition is improved, dehydration corrected and nervous tension abolished. A useful initial remedy is hydrocortisone 100 mg in 500 ml saline intravenously by slow drip. Cortisone in oral dosage of 200-300 mg daily gradually reduced to 12.5-50 mg for as long as the asthmatic tendency is present was until recently the most popular steroid medication. Prednisone and methylprednisolone are equally effective in about one fifth of the cortisone dosage range and minimal dosage may be continued for months if necessary.

Bronchiectasis

Study of the aetiological background will frequently provide helpful information. Such details as a history of bronchopneumonia or inhaled foreign body are not without significance. Congenital cystic disease, pulmonary collapse from bronchial neoplasm and coexisting tuberculosis are possible factors. Clinical examination supplemented by bronchoscopy and bronchography gives indication of the location and extent of the bronchial dilatation. The pulse and temperature record, leucocyte count and erythrocyte sedimentation rate enable the physician to assess toxic factors.

Medical treatment is palliative but should be used in every case. The patient should have rest in bed in the open air during mild weather. When he becomes afebrile suitable activities may be resumed. A liberal nourishing dietary is important as most bronchiectatics are toxic and debilitated. Iron tonics and fish liver oil preparations are valuable. The disease may be aggravated by exposure of the oropharynx and nasal sinuses and such should be attended to.

Postural drainage The penetrating factor of the sputum is largely due to the retention factor and drainage is encouraged by postural coughing several times daily. Posture slapping percussion and cough exercises are very much the province of a skilled physiotherapist. For basal bronchiectasis the patient should lie over the edge of his bed with the head hanging down. This will induce coughing and he then turns on the side of the sound lung. Apical cavities are drained by sitting upright and leaning away from the side of the affected lung. Lateral cavities are drained by lying horizontally on the sound side and afterwards hanging over the side of the bed. Postural drainage beds are available in most hospitals. The amount of sputum should be recorded daily. Bronchoscopic drainage is a useful pre-operative routine.

Expectorants with the exception of the morning saline draught are useless. Penicillin and streptomycin by injection have considerable palliative value and they (or the broad spectrum antibiotics) should be used during periods of acute pneumonitis and as a preparatory measure where operation is contemplated. Blood transfusions play an important part during the operative phase.

Surgical treatment Modern diagnostic procedures facilitate recognition of the disease at an early stage when radical cure is comparatively free from hazard and often brilliantly successful. Lobectomy and segmental resection are the operations of choice and in capable hands yield good results in cases of unilateral disease particularly in children and young adults. Bilateral segmental resection is occasionally feasible but cases with extensive bilateral lesions are unsuitable for surgery.

Pulmonary Abscess

Significant ætiological conditions must be sought for. Inhalation of infected material after tonsillectomy and dental extraction accounts for a proportion of lung abscesses. Suppurative pneumonias e.g. those due to *Klebsiella* and staphylococcal infections tend to excavate and pre-existing diseases such as bronchial neoplasm infarct and bronchiectasis are frequently associated with lung abscess.

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Systemic resistance should be improved by nourishing food, rest in bed in the open air and tonics. The sputum should be cultured and the appropriate antibiotic administered (usually penicillin). Thus the suppurative process may be limited and septicæmic complications prevented.

Bronchoscopy and bronchography provide an exact regional diagnosis. Foreign bodies of suitable size may be extracted endoscopically and suction drainage of the abscess cavity inaugurated. Postural drainage is sometimes effective and in conjunction with inhalation therapy and systemic antibiotics may keep a small abscess cavity empty enough to permit healing. Thick walled cavities must be dealt with surgically. Thoracotomy with dissection of the fibrous cavity lining and packing will give excellent end results in many cases. Lobectomy offers a prospect of cure in chronic and extensive abscess formation.

Pulmonary Infarction

Thrombotic forms are due to disease of the pulmonary artery with chronic venous congestion or to localised disease of the lung tissues. Embolic forms follow the impaction of wandering blood thrombi, fragments of valve vegetations, malignant metastases, fat or oil globules. Phlebotrombosis of the leg veins is by far the commonest source.

Absolute rest in the most comfortable posture should be adopted. Morphine gr $\frac{1}{2}$ with atropine gr $\frac{1}{100}$ is injected if there is much respiratory distress or chest pain. Large recommendations the intrapleural injection of 20-30 ml. of 0.5 per cent procaine which relieves pain and permits of normal respiration. Shock and collapse are met by stimulants such as nikethamide or an intravenous saline drip containing 1 mg adrenalin (4 mg to one litre). Oxygen inhalation is valuable particularly if cyanosis is present. Right ventricular defeat may occur in severe cases and must receive adequate treatment.

Pneumonia frequently supervenes and should be anticipated by the institution of suitable antibiotic measures.

Many pre- and post-operative routines have been devised to prevent venous thrombosis and pulmonary embolism.

Smoking should be given up for four to six weeks before elective surgery and adipose tendency corrected by suitable diet. While on the operating table the calves of the legs should be protected from pressure by pads of sponge rubber placed underneath. Fowler's position is conducive to venous stagnation and is an undesirable post-operative routine as ■ sitting slumped in an armchair. Frequent alterations of decubitus and encouragement of deep breathing and active muscular movements are of greatest importance ■ is correction of dehydration. The patient should be allowed to stand and walk and use the commode as soon ■ possible. These measures are particularly necessary in elderly obese and debilitated subjects and in those who have lost and had replacement of considerable quantities of blood. The incidence of embolism in such patients can be reduced by the wearing of elastic stockings while confined to bed as moderate compression improves the deep venous return from the legs.

Anticoagulant therapy Used prophylactically in predisposed cases or when the earliest signs of phlebothrombosis appear in order to encourage recanalisation.

Heparin Three doses of 12 000 i.u. of heparin intravenously at not less than six hourly intervals the third being given late in the evening. On subsequent days three or four doses of 8 000 units are used. After disappearance of pyrexia and of swelling from the phlebothrombotic site the dosage ■ reduced to two injections of 8 000 units daily for ■ few days. The patient should perform free muscular movements in bed and if practicable he ■ allowed up on the fourth day provided he wears an elastic bandage or Unna's paste sock on the limb to prevent oedema. If early ambulation ■ undesirable daily or alternate daily dosage with heparin is continued for two to three weeks. Dextran sulphate is replacing heparin in some clinics.

Coumarins After oral administration dicoumarol depresses hepatic synthesis of prothrombin by interference with vitamin K utilisation. For details of this treatment see page 241.

Trypsin Enzymic thrombolysis using specially purified trypsin for intramuscular injection is thought to be a more effective measure in thrombophlebitis than anticoagulants.

Surgical measures. Ligation of the common femoral or iliac veins is used in conjunction with anticoagulant therapy to prevent emboli spread to the lungs. Ligation of the inferior vena cava is a major project which will protect against pulmonary embolism. Crane (1957) lists three indications: pulmonary embolism from iliofemoral thrombosis where anticoagulant therapy has failed or is contra-indicated after femoral vein division and anticoagulants have failed; pulmonary embolism from septic thrombophlebitis.

Pulmonary Oedema

May arise from chemical irritation by failure of the left heart or as a terminal manifestation of renal disease. It is sometimes associated with coronary occlusion and allergic states. Treatment depends on the cause but must be prompt.

The patient should adopt the sitting position with the legs down. A hypodermic injection of morphine and atropine is given together with a slow intravenous injection of aminophylline 0.5 G. Venesection is often of benefit and continuous oxygen inhalation should be commenced. The latter is more valuable if humidified and given under positive pressure from an anæsthetic apparatus.

Luzzada postulates that the main cause of circulatory embarrassment from pulmonary oedema is the foaming propensity of the muco-serous transudate. Ethyl alcohol on inhalation has an anti-foam action. He advises inhalation by nasal catheter of a mist produced by passage of oxygen through 95 per cent alcohol.

Adequate digitalis must be given in cardiac cases particularly those with auricular fibrillation. In cases of recent cardiac infarction the oral route is safest and quinidine or procainamide should be given as well. In hypertensive left ventricular failure slow intravenous injection of a hexamethonium salt is indicated (bromide 5-15 mg.)

The allergic variety responds to adrenaline 10-20 minims by scattered subcutaneous dosage and an antihistamine e.g. chlorpheniramine. Puriton A & H 10 mg intramuscularly.

Pulmonary Atelectasis

The treatment of localised collapse is that of the primary condition usually bronchial obstruction. Management of a massive collapse likewise depends upon the cause. If due to wounds of the chest wall these should if practicable be treated by surgical toilet and closure if not tampon dressings are indicated. Those caused by collection of air or fluid in the pleural cavity are treated by aspiration and maintenance of normal intrapleural pressure. The incidence of post-operative pulmonary collapse may be reduced by the following precautions: cessation of smoking, correction of obesity and treatment of upper respiratory infections; patients with productive cough should undergo postural drainage for a few days; judicious premedication and choice of anæsthetic and terminal hyperventilation of the lungs with $\text{CO}_2\text{-O}_2$ mixture; relief of post-operative pain; prophylactic antibiotic routine when indicated by a debilitated or chesty patient; upper abdominal operation or swallowing difficulty; frequent change of decubitus.

The services of a skilled physiotherapist should be availed of for comprehensive muscular movements, forcible percussion over the lung bases and coughing exercises; the wound if abdominal being supported by the hands.

Bronchoscopic aspiration of tenacious bronchial secretion is helpful in severe cases.

Pulmonary Tuberculosis

The aims of treatment are

To improve nutrition and increase resistance

To destroy the tubercle bacillus and its toxic products

To promote resolution and healing of lesions

To alleviate symptoms

Measures which increase resistance include fresh air, nourishing food in liberal quantities and a judicious admixture of rest and exercise. A stay at a sanatorium benefits every consumptive not only from a therapeutic standpoint but for the inculcation of safe hygienic principles.

The regimen is much more important than climate or situation and there is much to be said for allowing the patient to work out his physical salvation in an institution close to his home. Febrile or toxic patients should never be allowed to journey to a distant sanatorium. Chronic fibroid cases require no treatment; they should be kept under supervision and if invalidism supervenes, be nursed in hospital.

Phthisical subjects should live as far as possible in the open air and those confined to bed may be wheeled on to sheltered balconies. Exposure to sunlight must be very gradual; otherwise reaction and hemoptysis may ensue. Pyrexia, rapid pulse rate and elevated erythrocyte sedimentation rate are indications of toxæmia and are met by absolute rest in bed. When these have subsided the patient then embarks on a carefully graduated course of physical activity. The first concession is being allowed to sit up in bed and feed himself and later to perform the toilet. When fever has been absent for two or three weeks sitting out of bed for half an hour is permitted and this is gradually increased according to circumstances. When he has reached the stage of being up and moving about for eight hours gentle exercise in the shape of a measured walk on the level is ordered and by suitable augmentations he is rehabilitated to six hours of strenuous work such as gardening, timber cutting and agricultural work daily. The pulse and temperature reaction to each grade of exercise is noted and any sign of intolerance is an indication for temporary rest, followed by relegation to a lower grade of activity. In view of the strain on sanatorium accommodation the preliminary bed rest must often be arranged in the patient's home.

In an illness of indefinite duration like tuberculosis mental stagnation must be discountenanced. Diversional therapy is begun at the stage of bed rest; occupational therapy, craft work and later scholastic, technological and social activities form an essential part of long-term treatment. By these means the patient may leave the sanatorium a more valuable economic unit than he entered it.

An appetising and nutritious dietary should be given. There is rarely any difficulty in persuading tuberculous patients to eat when they are living in the open air. Steady

gain in weight and reversion to normal sedimentation rate are indications of good progress. Hypochromic anaemia is common and should be treated with iron. Fish liver oils are useful in undernourished subjects provided that appetite and digestion are satisfactory.

Chemotherapy

Streptomycin The advent of this antibiotic has in fair measure realised the hope often confounded of a substance which would suppress tuberculous infection. Since its introduction to clinical practice acute milary tuberculosis has been moved from the hopeless to the curable category. Streptomycin influences favourably recent exudative lesions but the effect on fibro-caseous lesions is slight.

There are two important limitations to the efficacy of streptomycin namely the rapidity with which most strains of *M. tuberculosis* develop resistance and the toxic effects. The latter appear after heavy and prolonged dosage and usually during or shortly after completion of treatment. The vestibular irritation is often temporary but in any case compensation is achieved in time. Deafness is likely to be permanent.

Drug resistance can be delayed or prevented by combining streptomycin with *para* aminosalicylic acid and isoniazid. The adult dosage of streptomycin sulphate is 1 G daily intramuscularly for up to three months if more prolonged therapy is necessary the interval between doses may be increased e.g. 2 G twice weekly. Dosage for children 15 mg per kg body weight.

There is some evidence that smaller doses of streptomycin (in conjunction with PAS) are equally effective. 0.5 G daily or even 1 G every third day has been found satisfactory in all but relapsed cases. The present tendency is to extend antibiotic treatment over twelve to eighteen months according to progress.

***Para* aminosalicylic acid (PAS)** Used alone this drug has some value in human infections but in combination with streptomycin it has been proved to reduce the factor of resistance to both agents and there is believed to be an additive effect. Resistance to PAS develops but slowly and

is active against many strains which are streptomycin resistant. Adult dosage is 12.0 G daily orally in three divided doses. Dosage for children is 1 G per kg body weight daily. Nausea, vomiting and diarrhoea occur in over 50 per cent of cases. These may be mitigated by rearranging the doses in relation to meal or by using milk or aluminum hydroxide as vehicle. Rare toxic manifestations are hypoprothrombinæmia, anaemia, fever, psychosis and skin rashes.

Thiosemicarbazones Their action is comparable with that of PAS and they are popular in Continental clinics. The adult dose of Thiacetazone (Birculon, I.C.I.) is 100-200 mg daily by mouth. Toxic hazards are agranulocytosis and fatty hepatoses.

Isoniazid (Isonicotinic acid hydrazide) Attention was first drawn to its value in human tuberculosis by Selikoff and Robitzer (1952). This drug initiates dramatic improvement in the general condition. Appetite and weight increase, pyrexia and toxic manifestations lessen and the bacterial count of sputum is lowered. Unfortunately the clinical and radiological findings and E.S.R. are little altered. The organism acquires resistance within three to six weeks and the real rôle of isoniazid is as adjuvant to streptomycin. The adult dose is 100 mg orally twice daily. Children 3 mg per kg body weight.

There appears to be little advantage as between the combinations of streptomycin with PAS and with isoniazid. Isoniazid is a comparatively recent addition to the therapeutics of tuberculosis and its long term possibilities are still uncertain. Relative freedom from toxicity renders it a useful substitute for patients who cannot tolerate PAS in adequate dosage or where the organism has become resistant. J. H. Skadding (1955) regards PAS-INH as the best combination for out-patient treatment, especially in older age groups. In serious infections all three are given together.

Duration of treatment depends on the nature of the case and the response as judged by clinical and radiological findings. A good chemotherapeutic scheme is

1. Streptomycin daily for forty five days and subsequently every third day for another 15 injections (ninety days) combined with PAS daily.

2 Second course of streptomycin after an interval of two to four weeks PAS and INH daily for a further 90-120 days

3 A third course of streptomycin is given in most cases—over thirty days and subsequently every third day for another 30 injections (120 days) combined with INH daily

Chemotherapy is a valuable resource for quieting down the activity of recent cases who are clinically ill and toxic. It reinforces the good effect of conventional methods of treatment but is not a substitute for them. Miliary, pneumonic and soft exudative lesions, also laryngeal and tracheo-bronchial ulceration, respond best. Chemotherapy is of great value in cases likely to become suitable for surgical methods but it must be available as cover for the operative phase; if used prematurely the infecting organism may be resistant when protection is most necessary.

Surgical Treatment

Collapse therapy The object is to place the affected portion of lung at rest, thus encouraging fibrosis and collapse of cavities; this may be achieved temporarily by induction of pneumothorax or pneumoperitoneum or permanently by thoracoplasty.

Artificial pneumothorax The advent of effective chemotherapy and radical surgical measures has narrowed considerably the indications for pneumothorax treatment. It is no longer a first resort in early exudative cases but a second or third line of defence. Its main indication is for closure of small or medium sized soft-walled cavities in sputum-positive cases. Ideally the cavities should not be peripherally situated and should have a free bronchus. Also suitable for pneumothorax treatment are young adults showing good natural resistance rather than children or middle-aged adults. Fibrotic disease, large cavities, pleural adhesions, poor resistance with fever and raised ESR, and endo-bronchial lesions are contra-indications for pneumothorax. Satisfactory collapse should accrue within a period of four to six weeks. A pneumothorax which hangs fire requires positive pressures or is complicated by persistent pleural effusion is unsafe and should be abandoned in favour of other measures.

In a successful case the pneumothorax is maintained for 1½-3 years. There is no absolute indication as to when it may safely be terminated and the decision is usually made on clinical progress i.e. cavity obliteration sputum conversion.

Artificial pneumoperitoneum More frequently practised than pneumothorax as it is less liable to a complicated course. It has considerably wider application and in conjunction with phrenic crush induces effective collapse. It is useful during the chemotherapeutic phase of early cases and as it requires only modest technical resources it can be incorporated in the pre-sanatorium regime. It is also helpful in cases where pneumothorax has failed or would be likely to fail such as extensive cased-cavernous lesions, widespread pleural adhesion and recurrent pleural exudate. It is a useful temporary measure for patients who will require definitive surgical measures such as thoracoplasty or resection. It should not be used in cases with extensive fibrosis or with tuberculous abdominal lesions. Abdominal hernia is a contra-indication.

Phrenic crush Produces temporary paralysis and ascent of the hemi-diaphragm and is used mainly as auxiliary in pneumoperitoneum. Recent phrenic crush adds to the hazards of lung resection because of the increased risk of massive collapse.

Extrapleural pneumothorax Designed for cases where adequate intrapleural space cannot be found. The parietal pleura and the affected lobe are freed from the inner surface of the thoracic wall in the plane of the endothoracic fascia. *Plombage* with polythene sponge has proved a successful modification. Extrapleural fascial apicolectomy with *plombage* gives better results and has ousted thoracoplasty in some clinics. These procedures give good selective collapse and are used for apical cavities. Being one stage operations and causing no thoracic deformity they are popular with patients.

Thoracoplasty Secures permanent collapse in cases not suitable for other surgical procedures. This is the safest major surgical project provided that patients are carefully selected. Best results are obtainable in upper lobe cavities but cavities in other situations are often closable. It is also indicated for obliteration of pleural cavities following

empyema or pneumothorax it may be necessary in conjunction with resection operations to reduce the dead space. Thoracoplasty is not useful in cases with extensive bronchial involvement and large tension cavities nor in massive consolidative foci or mainly basal lesions. Elderly, obese and emphysematous subjects stand the operation badly and derive no benefit. The operation is a two-stage one, the upper 5-7 ribs being removed and the lung apex freed by extrapleural apicolysis.

Lung resection. Chemotherapy has greatly widened the possibilities for operations of this type and radical surgery bids fair to eclipse other techniques.

Indications

Extensive unilateral disease with or without controlled contralateral lesions

Large tension cavities particularly in the lower lobes

Bronchial stricture, bronchiectasis

Massive caseous involvement (tuberculoma)

Recurrent hemoptysis from apical cavity

Children and adolescents where deforming operations are inadvisable

Contra Indications

Streptomycin resistant cases

Extrapulmonary lesions

Poor vital capacity

Active endobronchial lesions

The operation may have the extent of segmental or wedge resection, lobectomy or pneumonectomy according to anatomical involvement. Complications are bronchial fistula and empyema.

Symptomatic treatment. For cough a warm saline draught on waking facilitates expectoration. Irritating and useless cough may disturb sleep and is best controlled by a sedative e.g. pholcodine 8-12 mg. in Simple Linctus B.P.C. The sufferer must acquire the art of coughing gently. Postural drainage is helpful in many cases. Night sweats are a sign of toxæmia and are lessened by rest in bed, fresh air and attention to skin hygiene. Anorexia arises from the same

cause and similar general measures should be invoked. Bitter tonics or a pre prandial aperitif are useful aids to appetite.

For laryngeal ulceration complete rest of the voice is desirable at first and the patient should communicate in mime or writing. When the condition has improved he may be allowed to converse in whisper. Aromatic inhalations such as Menthol and Eucalyptus Inhalation, B.P.C. from a Yeo's mask are soothing and reduce cough.

Lactic acid or Lake's paint may be applied to the laryngeal ulcers and cauterisation used in more advanced cases. If swallowing is difficult insufflation of a powder composed of equal parts of benzocaine and orthocaine before meals will reduce laryngeal irritation. Chemotherapy lessens the discomfort of ulcerative lesions even in presence of hopeless pulmonary involvement.

Tuberculous enteritis should be treated by rest in bed, high-calorie low residue diet and astringent mixtures. Helio- and ultra violet therapy are sometimes beneficial but they must be employed with caution. Streptomycin has been found helpful but its administration should be systemic rather than local. Ischio-rectal abscess and fistula in ano occasion serious discomfort and disability and radical surgical treatment should be advised in all but hopeless cases. For genito-urinary involvement the general principles of treatment apply and they should be supplemented by appropriate surgical measures.

Hæmoptysis. Complete rest in bed (prone and with the foot raised) and reassurance are important. Morphine gr. $\frac{1}{2}$ should be injected to calm the patient and stabilise the circulation. Food should be limited to cold fluids for twenty four hours. Styptics and hæmostatic sera are of no value but blood transfusion may be necessary following severe bleeding. Artificial pneumothorax is occasionally required to induce relaxation of a bleeding lung but pneumoperitoneum (1,200-1,500 ml.) is a safer alternative. Lung resection should be considered for recurrent hæmoptysis.

Spontaneous pneumothorax. If small calls for no special treatment. Extensive valvular types produce grave respiratory embarrassment and the intrapleural pressure must be

reduced to atmospheric. This may be done by needling using a water seal. Negative pressure methods are unwise.

Prophylaxis

Detection of infected persons in the early stages. Mass miniature radiography has proved of inestimable service in case finding. Notification of cases and intimation of suspects. Disinfection of premises and clothing. Hygienic disposal of sputum.

Isolation of all open cases. Sometimes difficult, particularly in chronic fibrotic cases. Economic stress may militate against the individual's chance of prolonged cure. Entitlement to allowances under the National Assistance Acts is a notable step, and the provisions of the Disabled Persons Employment Act are of great assistance in the economic rehabilitation of tuberculous wage-earners.

Sanatorium treatment for all cases likely to benefit, with efficient after-care. The self-supporting colony system, e.g. Papworth Village Settlement, is a practical solution of the economic problem. Here patients lead normal and productive lives together with their families. In such carefully controlled environment the risk to children of infected families is minimal.

Provision of training hostels, night sanatoria and supervision of chronic cases.

Clinical supervision of contacts, particularly young children, with preventorium treatment when necessary. Miniature radiography is useful for screening large numbers of contacts; suspects are afterwards subjected to full clinical and radiological examination. Routine Mantoux testing of child contacts indicates those already infected. Adult and elderly members of an infected household should not be excluded from the investigation.

Bacille Calmette-Guérin (B.C.G.) This preventive measure has gained world-wide acceptance. Intradermal inoculation by multiple puncture of a live avirulent strain of *Mycobacterium tuberculosis* (bovine) in tuberculin-negative subjects will provoke immunity and conversion of the tuberculin reaction, thus increasing resistance to infection with virulent organisms. Conversion is expected six to eight weeks after inoculation. Recently vaccinated subjects should be protected from

natural infection for at least three months. The duration of the resistance so induced has not yet been determined but it may last ten years. Attenuation of the vaccine is secured by cultural methods and one of the practical difficulties is to maintain a vaccine output of optimal virulence. Liquid vaccines must be used within a week of manufacture but freeze-dried preparations are free from this disadvantage. A Medical Research Council Committee reported that these induce almost as high a percentage of tuberculin sensitivity as the older vaccines but the observation period has been short.

Infants are vaccinated within a few days of birth and if belonging to infected homes they are segregated until basal immunity has been established (usually two to three months). Mantoux negative girls should be vaccinated at the age of 10 years on account of the risk of post-primary genital tuberculosis at puberty with subsequent sterility.

B.C.G. has special applicability in tuberculin-negative reactors who are exposed to unusual risks of infection: children of tuberculous parents, nurses and medical students.

Tuberculosis and occupation. Unless he has used the enforced leisure to fit himself for a better post-economic necessity will frequently compel the consumptive to return to his former occupation, however unsuitable. Open-air occupations are best provided they do not involve strenuous physical exertion or exposure to damp and cold. Open cases should not return to occupations in which they are liable to infect fellow-workers: nursing, teaching and food handling are particularly dangerous.

The need for prolonged medical supervision should be impressed upon the patient.

Tuberculosis and marriage. There is no contra-indication to marriage in the case of genuinely arrested tuberculosis. Other cases must be judged according to circumstances. The risk of infection of the healthy partner and of further breakdown and invalidism of the infected partner should be explained to both. Against these risks must be offset the manifold advantages of settled home life.

Tuberculosis and pregnancy. Women with active tuberculous lesions should in general avoid pregnancy, although

the risk of rapid deterioration following delivery has been exaggerated

In tuberculous women who are pregnant management depends upon whether the lesions are likely to be controllable if so treatment as outlined above is a matter of urgency. The only modification would be that major surgery should not be attempted during the last trimester. Therapeutic abortion may be indicated in wholly unpromising cases but it should be undertaken within the first twelve weeks of pregnancy. In quiescent cases pregnancy is usually uneventful provided that reasonable precautions are taken.

A decision regarding breast feeding must depend on individual circumstances. If the tuberculosis has been quiescent for two years and the domestic situation is good there is no objection. If home conditions are poor and the mother's responsibilities numerous or if she is receiving pneumo-collapse therapy lactation is unwise.

The infant should receive B C G vaccination.

Sarcoidosis

The relationship of this condition to tuberculosis is obscure many patients fail to react to tuberculin although some develop tuberculosis eventually.

Epithelial cell granulomata occur in the liver lungs lymph glands skin and small bones of the hands and feet. Myocardial and renal involvement are not uncommon. A similar pulmonary fibrotic picture occurs in berylliosis and histoplasmosis.

Prednisone is indicated where the disease is rapidly progressive and may have to be given indefinitely. As infection with tubercle bacillus may also be present it is essential that antituberculous therapy be given at the same time.

Pulmonary Fibrosis and Pneumoconiosis

The former designation includes many different types of lesion such as fibrosis following bronchopneumonia or chronic pulmonary infections the latter is associated with inhalation of irritant dusts.

Fibrosis following infection is treated on the lines indicated for chronic bronchitis. For pneumoconiosis exposure to the

irritant atmosphere should cease. A quiet open air life in a dry equable climate is beneficial and all measures likely to improve nutrition should be adopted. Symptomatic treatment as for chronic bronchitis, emphysema and cor pulmonale should be given. Severe dyspnoea and bronchospasm are relieved by prednisone 30 mg daily and gradually reduced to 5-15 mg.

Prophylaxis of pneumoconiosis consists of regular radiological examination of those at risk with exclusion of employees showing even slight signs or symptoms of pulmonary disease. Certain precautions are enforced e.g. provision of respirators, efficient local exhaust ventilation, wet unloading and grinding.

Silicosis. Silica is the noxious agent common to gold and anthracite mining, sandblasting, asbestos handling and certain processes relating to iron production. Silicosis is frequently associated with tuberculosis and the disability may be progressive after the dust factor has ceased to operate.

On inhalation silica particles are carried into the tissue spaces of the lung stroma by dust cells. Here a silica colloid is formed which is toxic to pulmonary tissue. Experimentally a finely particulate aluminium inhalation or one charged with a solution of calcium coats the silica crystals with a protective layer of hydrated alumina or lime which inhibits fibrous reaction to quartz. These methods have not proved acceptable in practice.

Intrathoracic Neoplasm

Benign tumours and cysts arising from nerves, ribs, pleura, mediastinal tissues or bronchi can be removed surgically. Bronchial carcinoma is by far the commonest intrathoracic tumour. Early diagnosis is important as pneumonectomy with lymphatic dissection may be curative in suitable cases. Radiotherapy is used as auxiliary to surgical extirpation or as a palliative in inoperable cases.

Pain and cough are usually troublesome and call for analgesics or sedation with pholcodine, morphine, pethidine or dihydrocodone bitartrate (DF 118, dose 30-50 mg subcutaneously, 30 mg orally). Pleural effusion should be

aspirated air replacement is sometimes of service in management of recurrent effusion

Pleurisy

Dry pleurisy should be treated by rest in bed and light diet. Pleural pain is usually prominent at the outset and may be lessened by strapping the affected hemithorax. Heat in the form of kaolin poultices or short wave diathermy is preferable in many cases. For irritating and painful cough a sedative linctus may be employed.

In the stage of effusion treatment is directed to promotion of absorption of the exudate and re-expansion of the affected lung. Diet may be increased as the fever moderates and tonics of iron and vitamins are valuable. Rest should be continued and in the open air if possible for three to six weeks after pulse, temperature and F.S.R. have regained normal. Deep-breathing exercises and Woulfe's bottles are useful for promoting re-expansion of the collapsed lung. A diagnostic paracentesis is desirable as the information thus obtained will be helpful in designing further treatment.

Small and moderate effusions often absorb spontaneously but aspiration is necessary in the following circumstances:

- 1 The effusion is large or accumulating rapidly causing respiratory difficulty
- 2 There is no evidence of absorption after two to three weeks
- 3 The effusion is bilateral
- 4 The effusion is purulent
- 5 The effusion complicates an active tuberculous lesion (artificial pneumothorax may be indicated)

In the first and second groups removal of 10-15 oz. of fluid will often relieve symptoms and initiate spontaneous absorption. Complete evacuation of the exudate will be necessary later if absorption is tardy or reaccumulation occurs. Unduly rapid removal of large amounts of fluid is contra-indicated on account of the danger of mediastinal shift and premature aspiration appears to encourage further exudate.

The aetiological basis of the pleurisy must be taken into account when elaborating further treatment. Those complicating acute lung infections require treatment of the primary condition. About 30 per cent of idiopathic pleurisy cases subsequently develop pulmonary tuberculosis and it must be assumed that those occurring in young persons are of tuberculous origin. Some settle only after a course of anti-tuberculous drugs. Radiography of the expanding lung may demonstrate an active focus and such cases should have prompt sanatorium treatment. Others should be treated as suspect tuberculosis and given a prolonged holiday with nourishing food and vitamin preparations. Regular clinical and radiological supervision should be available for five years.

Empyema

Usually secondary to inflammatory lung disease and the primary condition should have appropriate treatment. Bacteriological diagnosis will furnish indications regarding appropriate chemotherapeutic measures. Systematic penicillin is valuable at the outset of most pneumococcal, streptococcal and staphylococcal infections of the pleura. The effusion should be aspirated daily or every two days and 500 000 u.u. of penicillin in 15-30 ml of sterile saline injected until bacteriological findings become satisfactory. Streptomycin (150-200 mg.) may be similarly used in the presence of organisms sensitive to this drug although its bacteriostatic effect in pus is inferior to that of penicillin. The broad spectrum antibiotics should be administered systemically when particularly indicated.

Medical treatment of empyema although rarely adequate alone is a desirable preliminary to surgical drainage and toilet of the pleura. If the empyema is encysted or localised to a lung fissure aspiration may be difficult and early drainage is required. Pus of a non-aspirable consistency is an indication for several daily or alternate daily injections of streptokinase & reptodornase intrapleurally. These enzymes liquefy fibrin clot and thick pus and are used in doses of 20 000 and 5 000 u.u. respectively. Decortication is indicated when the lung is bound down by a thick fibrous covering.

Pyopneumothorax usually results from drainage of an empyema through a bronchus or rupture of a lung abscess. Pleural fistula may follow empyema necessitatis. For these prompt surgical treatment is necessary.

Pneumothorax

When associated with a penetrating chest wound requires treatment of shock. Later removal of foreign bodies, blood clot and lacerated tissues should be followed by careful repair of the chest wall and finally aspiration of imprisoned air. Penicillin by local and general administration is an invaluable auxiliary to the surgery of chest wound.

Spontaneous pneumothorax may appear in apparently healthy chests and in the absence of any exciting cause such as physical exertion. Non tuberculous pneumothorax is often due to rupture of an emphysematous bulla or pulmonary cyst. The condition tends to recur and in a small proportion of cases pulmonary re-expansion is delayed.

If the effusion of air is small rest in bed and the administration of an anodyne will be sufficient. Valvular types cause mediastinal shift and great respiratory distress the air should be allowed to escape through a chest needle connected to a rubber tube the free end of which is immersed in water thus limiting the intrapleural pressure to atmospheric. This may be dispensed with as soon as the rent in the lung has become sealed.

Recurrent cases should be investigated by bronchography and thoracoscopy as treatment depends on the cause. A cystic condition calls for localised excision or lobectomy. emphysematous cases with a free pleura are submitted to pleurodesis (instillation of silver nitrate 5-10 minims of 10 per cent solution intrapleurally).

Spontaneous pneumothorax may complicate pulmonary diseases notably tuberculosis (see p 279).

Congenital Cystic Disease of the Lung

May communicate with a bronchus or rarely be non communicating. The latter is symptomless unless rupture occurs. The former may show a solitary cyst, a cluster of small cysts or a large balloon cyst. Symptoms may be

absent or dyspnoea may be a feature. Haemoptysis, spontaneous pneumothorax and infective complications such as lung abscess, bronchiectasis or empyema are liable to supervene.

The balloon cyst is caused by the check valve action of a bronchial kink and may give rise to urgent respiratory distress which is temporarily relieved by needling. There is danger of development of tension pneumothorax after needling and surgical resources for this emergency must be at hand. Resection of the cyst or lobectomy is the only satisfactory measure. The complications mentioned above call for appropriate remedies.

Treatment is otherwise concerned with maintenance of general health and careful attention to upper respiratory infections.

CHAPTER XV

DISEASES OF THE NERVOUS SYSTEM

Peripheral Nerve Lesions

Localised lesions of peripheral nerve trunks may arise from direct trauma, compression or from traction injury. Medical treatment is directed to maintaining the nutrition of the weakened muscles and preventing contracture and deformity. These principles are secured by application of suitable splintage and this should be easily removable to permit the use of physiotherapy. Massage and full movements of the affected limb are given daily. Electrotherapy is useful when signs of nerve regeneration appear.

If no improvement results after a period of several months surgical treatment must be considered. Exploration of the affected nerve trunk and freeing it from scar tissue or if continuity is interrupted restoration by suture are useful.

Russell Brain and Dickson Wright have described a syndrome due to spontaneous compression of the median nerve in the carpal tunnel and characterised by wasting of the thenar eminence, weakness of the abductor pollicis brevis and opponens pollicis and sensory changes of median distribution. Surgical division of the anterior carpal ligament is curative.

Multiple Neuritis Peripheral Neuropathy

The classical type arising from toxic state or nutritional defect shows symmetrical and peripheral distribution with considerable subjective sensory upset. After removal of the cause the paresis and trophic disturbance are usually reversible. Characteristic muscle group involvement distinguishes other specific entities like diphtheria, leprosy, plumbism and the collagen diseases.

General management consists primarily of dealing with the cause or the underlying disease. Lead poisoning responds

well to treatment with sodium calciumedrate (see p 87) while gold and arsenical toxicity improves with BAL therapy (see p 330) Thiamine deficiency arises through deprivation or more usually from alcoholism where the deficiency is associated with inhibition of the pyruvate oxidase system and high blood pyruvate levels Thiamine 20-30 mg daily intravenously at first is useful only within its narrow indication, and neuropathy due to lewisite or toxic and other metals is not improved by vitamin B dosage

Polyneuropathy associated with carcinomatosis and porphyria has no specific remedy but should be treated on general principles that found in Addisonian adrena improves *pari passu* with the haematological response to cyanocobalamin Diabetic remittis is an indication for careful stabilisation of the metabolic condition

Bed rest is essential until the attack has spent itself and regression appears Nourishing dietary fresh air cheerful surroundings and diversional therapy are very desirable Anaemia should be corrected and anodynes like aspirin codeine or Dover's powder prescribed for relief of pain especially night pain Chlorpromazine (Largactil M & B) is useful in the early stages in dosage of 25-50 mg by mouth twice or thrice daily Corticosteroids and the steroid hormones give good results in some cases particularly where the neuropathy is severe and extensive in these there is presumably an allergic factor or gross toxic basis

Local treatment That of muscular paralysis in general Affected limbs are placed in a position of physiological rest and light splintage sandbags and bed cradles should be employed Heat as infrared radiation or hot stupes is soothing and relieves pain allowing a full range of passive movements to be done daily Later light massage and assisted voluntary movements are introduced, graduating to movements against resistance The use of a warm bath or whirlpool improves the blood supply and makes all muscle movements easier Re-educational exercises help to regain lost skills

Various types of neuropathy with emphasis on sensory disturbance have been described e.g. Refsum's syndrome H. Garland (1950) has reported cases with motor loss

suggestive of spinal cord involvement and cerebral neuropathy due to vitamin B₁₂ lack has recently been recorded

Acute febrile polyneuritis (Guillain-Barré syndrome) There is usually a history of an acute febrile illness followed by paraesthesia and muscular weakness which beginning in the lower limbs spread upwards to involve the trunk musculature and the cranial nerves facial and bulbar palsies and diplopia are especially common Thus rapidly ascending palsy of Landry type may simulate poliomyelitis and acute porphyria may present a similar clinical picture There is no specific treatment Bladder distension calls for catheterisation and if persistent for continuous catheterisation or tidal drainage Should respiratory failure threaten the patient must be placed in a mechanical respirator the airway kept clear and oxygen inhalations given Palatal weakness or difficulty in swallowing is an indication for tube feeding Prednisone by mouth (60 40 and 20 mg on the first to third days and then tapered) is of value during the acute stage Hyperkalaemia occurs from muscular tissue breakdown and should be corrected Local treatment is as described above

Neuritis

Sciatica and brachial neuritis were formerly thought to be caused by acute interstitial neuritis or primary inflammation of the nerve coverings with secondary involvement of the parenchyma The great majority of such cases are due to protrusion of the nucleus pulposus of an intervertebral disc giving rise to direct pressure on the nerve root Interstitial neuritis is seen in leprosy as an occasional manifestation of rheumatic disease or as the result of a nerve being involved in an area of sepsis It may also arise from compression or repeated minor trauma e.g. radial palsy external popliteal paralysis

Localised neuritis of the shoulder girdle Severe pains in the affected shoulder usually herald the atrophic paralysis which affects most commonly the serratus anterior spinati deltoid and biceps About one half of the cases are found in patients hospitalised for some other disease some cases develop spontaneously but in others there may be a recent

history of pneumonia surgical operation or blood transfusion circumstances which suggest a virus origin The condition resembles closely the neuritis which may follow the injection of serum e.g. antitetanic antidiphtheric The long term prognosis is good although recurrence has been noted

For the severe initial pains aspirin alone or in combination with phenacetin and codeine should be given With the appearance of paralysis the arm should be supported by a splint so that the affected muscles are in physiological rest the splint is removed daily for full passive movements When the acute phase has subsided daily massage galvanic stimulation and later active movements and exercises are given until there is recovery of voluntary power

Brachial neuritis Often attributed to sitting in a draught or excessive muscular exertion In many cases the application of radiant heat followed by vigorous massage of the stiff and painful muscles may suffice to bring about a cure When the pain persists or recurs the cervical spine should be radiographed In a high proportion of cases especially the middle aged and elderly there is evidence of osteoarthritis or of prolapse of an intervertebral disc The sixth cervical disc is commonly involved causing irritation of the seventh cervical root

The most effective treatment in such cases is absolute rest in bed for three weeks The head should be supported on one or two pillows with the patient recumbent and fully relaxed Aspirin phenacetin and codeine are required at first for the pain but as a rule this quickly disappears Meprobarn (Mylanexin elixir B.D.H.) in doses of one drachm four times daily is sometimes useful in promoting muscular relaxation When pain subsides passive movements of the neck and gentle massage should be given When allowed up the patient should be advised to return gradually to normal activities and for a time to rest supine for an hour each day In some cases especially when pain has recurred it may be advisable to order a collar of plastic or leather to be worn for some months Surgical treatment by decompression of the affected nerve root or excision of the prolapsed disc is rarely necessary except in cases of high cervical disc prolapse

Cervical rib Many are symptomless and discovered accidentally. Operative treatment should be considered in cases showing signs of recurrent vascular symptoms or neurological disturbance with pain, muscle wasting or sensory loss in the ulnar distribution. Various types of abnormality are encountered and the compressing surface whether a seventh cervical rib, normal or rudimentary first dorsal rib, a fibrous tissue attachment or an abnormal scalenus should be removed. The operation of division of the scalenus anticus is reputed to relieve pain by allowing the first rib to drop, but its main indication is compression of the subclavian artery. Mild cases should be treated by splinting the arm at a right angle to the trunk. Exercises to set up the shoulder girdle and to strengthen the trapezius are of value as they are also in many pregnant or middle aged women complaining of intractable pain with drooping of the shoulder girdle on the affected side. Shoulder dragging as in carrying heavy weights should be avoided.

Sciatica A generic term which includes the much disputed primary sciatic neuritis and lesions which are compressive in type.

Organic disease of other systems must be excluded e.g. diabetes. Pott's disease. Pelvic examination should be done to exclude the presence of neoplasm. Radiography of the spine and pelvis will reveal the presence of spondylitis, spondylo listhesis, sacro-iliac joint affection or malignant metastasis. Spinal root pressure from an intervertebral disc lesion is the commonest cause of sciatica. The discs degenerate in middle age and slight trauma in the shape of a heavy lift with the spine flexed will cause rupture of the annulus and posterior or lateral protrusion of the nucleus pulposus. All the neurological signs formerly attributed to sciatic neuritis such as pain on stretching the nerve, loss of ankle jerk, sensory impairment and muscular wasting are reproduced by disc lesions. The most commonly protruded disc is L5—S1 (1st sacral root). L4-5 (5th lumbar root) is next in order of frequency but lesions of the 2nd and 3rd lumbar disc also occur. O'Connell has associated maternal obstetrical paralysis with rupture of the 5th lumbar disc and compression of the cauda equina.

The most important ingredient of treatment in sciatica is complete rest in bed. This is maintained until pain and tenderness of the nerve trunk have disappeared. The patient should be kept comfortably warm and encouraged to assume the position of greatest ease the affected limb being supported by pillows. Aspirin with codeine, phenacetin or phenobarbitone is usually effective. Panadol Bayer and Proponesia B D H are useful proprietary alternatives dosage up to 8 tablets daily. The local application of heat is soothing e.g. well protected hot water bottles, hot stupes, radiant heat lamp. Myanesin may help muscular relaxation as recommended in page 291.

The patient should not be allowed up until he has been free of pain for some time and it is important at this stage to massage the muscles and to give active exercises in standing and walking so as to correct any faulty postural tendencies. When pain has been very severe and prolonged and there have been previous attacks it is advisable to follow up the rest period by a term in a well fitting plastic jacket which is worn for some months and renewed when it works loose. Spinal manipulation, stretching the nerve under anaesthesia and epidural injection have fallen out of favour.

Surgical treatment in the form of excision of the herniated disc is indicated when there are definite signs of nerve root irritation or compression, pain persists in spite of rest or when it recurs after an adequate trial of conservative measures. As might be expected in such a tedious and painful malady the results are not uniformly successful. Even when before operation the signs have been unequivocal pain may recur when the patient undertakes undue physical exertion but in many cases there is gratifying relief after operation. Psychological factors should be considered, although the mistake must not be made of allowing the intensity of a patient's emotional reaction to severe pain to deter one from advising operation when this is clearly indicated. Great caution is however necessary in reaching this decision in cases in which there are hysterical features or where there is a history of industrial injury and the question of compensation arises.

Referred sciatic pain is sometimes a symptom of severe lumbar fibrositis (myofascial sciatica) treatment is as for lumbago (p. 334). Osteoarthritis of the hip joint and lumbosacral or sacro-iliac strain often cause symptoms which are mistaken for sciatica. Joint strain may be relieved by mechanical support, as by carefully fitted belt or corset.

Anterior crural (femoral) neuritis. Usually a symptom of lumbar spondylosis or nuclear herniation but occasionally the nerve trunk becomes involved in a local inflammatory process. Symptomatic treatment is as for sciatica.

Paraplegia

Treatment depends on whether the onset of paraplegia has been recent and acute or slowly progressive.

Acute paraplegia. This may be due to myelitis complicating such virus diseases as measles, smallpox and vaccinia or disseminated sclerosis and neuromyelitis optica. Acute necrotic changes in the cord may result from syphilitic endarteritis or obstruction of vessels in the epidural space by new growth or abscess. The recognition of the latter at an early stage is of special importance for if operation is delayed until signs of paraplegia have appeared prospects of recovery of function are poor. Paraplegia may develop rapidly in spinal cancer. In the absence of knowledge regarding the cause treatment in acute myelitis is symptomatic.

Distension of the urinary bladder must not be permitted. Retention with overflow is usual at first but in favourable cases some degree of automatic control is gained. Bladder contractions may be reflexly stimulated by stroking the soles of the feet or it may be possible to express urine by gentle manual compression of the bladder through the abdominal wall. Usually regular catheterisation or tidal drainage by a self retaining catheter is necessary. Cystitis should be combated by free intake of fluids and trisulphonamide tablets or a suitable antibiotic. When there is accumulation of pus bladder washes using weak antiseptics such as boric acid or 0.1 per cent acriflavine are required. Prolonged recumbency and infection both favour calculus formation. Frequent changes of posture, abundant fluid intake and an acid ash diet are indicated.

As regards care of the bowels once a week a soap and water enema should be given followed the same evening by an aperient. This inevitably leads to soiling of the skin and bed the next day but when satisfactory evacuation is attained the bowels require little attention for the rest of the week. Thus frequent skin contamination is avoided. Abdominal distension due to gaseous accumulation (when not due to impaction of faeces in the rectum) is relieved by the hypodermic injection of 0.5 mg. prostigmine methyl sulphate.

Careful nursing to keep the undersheet free of creases, the skin clean and dry and frequent changes of posture are essential. An alternating pressure point mattress (Tasley) is useful in preventing decubitus sores in helpless patients. These measures alone often fail to prevent pressure sores in high spinal cord lesions (above T6) where there is absolute loss of all functioning below that level. Vasomotor paralysis of the superficial vessels supplying the skin probably explains the rapidity with which pressure sores can develop through initial small areas of necrosis, the result of ischaemia. In such cases the patient's position must be changed very frequently and it is not sufficient to turn him only from side to side. For the greater part of the time he should be raised in the supine posture on a spinal bed built up with layers of extra pillows for convenience. Nursing in this fashion becomes all the more essential once pressure sores have formed over the sacrum and other sites. After preliminary saline soaks penicillin-sulphadiazine powder should be applied under a plain dressing such as soft paraffin gauze and the pressure sore then sealed off by the application of a wide strip of elastic adhesive. The haemoglobin and plasma protein levels must be watched and repeated transfusions of whole fresh blood, oral administration of 100 mg. ascorbic acid daily and a diet rich in protein (100-150 G. daily) are the best means of securing rapid healing of indolent chronically infected sores. Testosterone propionate 25 mg. by muscle at five-day intervals or androstanolone Anabolex, Lloyd Hamol 2.5 mg. Tablets sublingually daily will encourage nitrogen retention. When sepsis has been overcome skin grafting may be desirable to speed healing.

As regards posture of the paralysed limbs the knee joints should be kept extended and the ankles dorsiflexed any tendency to outward rotation of the limbs being checked. Daily passive movements through a complete range in each joint are required and light massage should be given to hypotonic muscles. The upper limbs when paralysed should be rested in a position of extension at the elbow joints and wrists. Any tendency to flexion contraction of the fingers should be counteracted by the use of sponge rubber fixed in position in the palm of the hand.

Chronic paraplegia. Although in paraplegia of acute onset signs of total loss of spinal cord function may persist it is usual to find some recovery of vasomotor tone. Thus even with high thoracic lesions after a time the patient can sit up without fainting. The usual nursing precautions will then be sufficient to prevent pressure sores even though sensation is still defective. The patient may be taught to balance himself sitting upright by utilising muscle above the level of the lesion e.g. latissimus dorsi and suitable patients may gradually proceed to walking with the aid of calipers fitted to the legs and elbow crutches.

The most difficult problem in chronic paraplegia is spasticity. Flexor spasms increasing in strength and frequency herald the development of paraplegia in flexion. They are made worse by massage but relieved to some extent by small doses (gr. 1) of sodium amytobarbitone or codeine $\frac{1}{2}$ gr. Mephenesin (Myanesis $\frac{1}{2}$ gr. \equiv D.H.) 1 drachm or quinine sulphate gr. 2-3 thrice daily may be tried. Nursing the patient on alternate days in the prone and supine positions with cradling is of value but whenever possible attempts should be made to get the patient to stand. When the upper limbs are unaffected this may be done by placing him between parallel bars situated at hand level and encouraging him to keep the legs extended whilst at the same time he distributes his weight between the arms and legs. When sensation is little impaired these exercises may be undertaken under water in a deep pool bath the patient supporting himself on handrails under the direction of the physiotherapist. The walking chair is another useful apparatus for patients afflicted with spasticity. Remarkable

rehabilitation may be achieved when the underlying lesion is inactive and has been successfully dealt with e.g. extra medullary spinal cord tumour

Ataxic paraplegia due to the partial cutting off of proprioceptive impulses from disease of the posterior columns may be greatly benefited by the re-education exercises of Frankel. These are aimed at teaching the patient to control the movements of his limbs under the direction of the eyes by walking beside a handrail and placing the feet as accurately as possible on footprints painted on strips of canvas or rubber.

Disseminated Sclerosis

There is no specific treatment the cause underlying the recurring episodes of patchy demyelination being as yet unknown. Cloake advocates treatment with the organic arsenicals over a period of several years. Histamine is favoured by some for treatment of relatively fresh episodes (1 mg. of histamine base in 250 ml. of normal saline intravenously rapidly to induce facial flush but no headache). Amyl nitrite inhalations have been used for the same purpose. There is no defect in glial formation and no convincing evidence in favour of trace element deficiency e.g. copper cobalt. Swark suggests restricting fats and meat and allowing a high carbohydrate diet. Care should be taken in all cases of disseminated sclerosis to avoid unnecessary confinement to bed—surgical operations should not be undertaken unless essential. Treatment of the paraplegic state is described in page 294.

Subacute Combined Degeneration

Treatment is by vitamin B₁₂ (cyanocobalamin) as in Addison's anaemia but much larger doses are required. It is not enough to restore the blood picture to normal. Intensive treatment should be continued as long as there are signs of improvement in the neurological state. The postero-lateral cord changes are irreversible but when an early diagnosis is made the signs to which they give rise will not present any bar to successful rehabilitation on the lines described for chronic paraplegia (see p. 296). The dosage of cyanocobalamin should be 1000 mg. by muscle every other day for 6

doses then a similar dose bi weekly for 6 weeks a basal dose of 20-100 mg. weekly or fortnightly may suffice Distivite 3 100 μ g tablets daily is reputed equally effective

Syringomyelia

The patient should be warned against the danger of septic infection of the hands and of injury e.g. burning or scalding Deep x ray treatment to the spinal cord is said to have some effect in retarding glial proliferation but the results are variable and inconclusive occasionally when pain is a prominent symptom it may help Laminectomy with incision of the cord and drainage of a distended cavity has been performed in cases in which the signs point to rapidly increasing compression But these symptoms often subside spontaneously and surgical intervention is seldom justified

Amiotrophic Lateral Sclerosis

In most cases death results within three years from the onset Few patients with bulbar complications survive longer than one year When muscular wasting is limited to the extremities progress may be slow and appear to be arrested for a time There is no specific treatment Bulbar cases require careful spoon feeding with semi solid foods mixed with liquids In advanced cases the only safe way of feeding is through a nasal tube passed into the stomach Dribbling of saliva may be checked by 5-10 minims of tincture of bella donna twice daily or atropine sulphate parenterally if swallowing is difficult

Hereditary Ataxias

Treatment has little effect on the course of these malades Attention to the general health encouragement of suitable activities and re-educational exercises may help to stave off serious invalidism (See under cerebral palsy) Orthopaedic appliances may be worn to overcome the troublesome lower limb deformities

DISEASES OF THE MUSCLES

Muscular Dystrophy

Vitamin E amino-acids and glycine have been used in treatment but the evidence in favour is unconvincing

Periodic rest and massage are helpful, but it is unwise to keep patients in bed for long as this increases disability. Deformities of the lower limbs may be corrected for a time by light splints, tenotomy or surgical boots. The chronic myopathy occasionally seen in association with thyrotoxicosis is said to improve after thyroidectomy.

Myotonia. In myotonia congenita and to a lesser extent in dystrophia myotonica quinine has a beneficial effect. It may be prescribed in doses of gr 10-30 of the hydrobromide daily.

Periodic Paralysis

It appears that there is no simple relationship between plasma potassium and muscular paralysis. Conn's work showed that attacks of paralysis spontaneous and induced were preceded by increased aldosterone secretion. The sodium content of muscle was greatly increased and the potassium unchanged. Recovery was associated with massive diuresis and sodium output. The cause of the intermittent aldosteronism is uncertain.

In the rare familial form the attacks are most severe in youth. Characteristically there is flaccid paralysis of the extensor muscles of the limbs on waking and it may be induced by cold, injection of adrenaline, the ingestion of glucose or a mainly carbohydrate diet. Tetany is sometimes present. The serum potassium level is usually drastically reduced during the attack and prevention is by the daily administration of potassium chloride 3-10 G in enteric coated capsules. During an attack, if respiration is affected it will be necessary to place the patient in a respirator. If he can swallow 1-2 teaspoonfuls (4-8 ml.) of 25 per cent. solution of potassium chloride in a flavoured vehicle should be given, otherwise 100 ml. of 1 per cent. solution of potassium chloride should be injected intravenously.

Alarming ascending flaccid paralysis may occur in hyperkalemia which may arise as a complication of chronic nephritis and is characterised by specific electrocardiographic changes (absent P and high T segments with increased S-T deflection) and high serum potassium level. Sudden death may result from heart failure if the condition is not promptly

or lingering doubts he may have regarding his fitness. Failure to take such steps and the creation of a wholly unnecessary atmosphere of fussy or solicitous attention often leads in neurotically predisposed persons to the development of post traumatic neurosis.

When loss of consciousness is prolonged the existence of cerebral contusion or other structural changes in the brain may be confidently assumed, and the degree gauged to some extent by estimation of the level to which consciousness has been restored when the patient is first seen. He should be nursed in the lateral decubitus without pillows and with the foot of the bed raised in order to prevent inhalation pneumonia. A constant watch must be kept and hourly observations made of the behaviour, size of the pupils and pulse and respiratory rates. The bladder is emptied by catheter, the mouth swabbed out and fluids given regularly through an oesophageal tube.

In certain cases of severe head injury where profound coma with hyperthermia and signs of embarrassment of vital centres present artificial hibernation may be employed. Chlorpromazine (Largactil M & B) is given initially 200 mg intravenously in saline over a period of three to four hours followed by intramuscular dosage with 50 mg and pethidine 50 mg as required. The patient is covered with a wet sheet and packed around with ice bags so that the rectal temperature is kept at 27-30°C for several days. This treatment produces marked lowering of intraventricular pressure with lessened tendency to intracranial bleeding. The method is especially valuable in high intracranial pressure hence its use in cases of cerebral tumour before and during operation in subarachnoid bleeding and morphine and barbiturate poisoning. Other indications for hypothermia are acute thyrotoxicosis, severe heat effects and hypertensive crises.

In favourable cases coma gives place to restless movements which gradually become more purposeful until the patient will answer simple questions. At this stage noisy delirium may be troublesome. It is best controlled by the intramuscular injection of 2.5 ml of paraldehyde, this dose being repeated as required. Morphine should not be given on account of its tendency to increase intracranial pressure. If

paraaldehyde 1 dr to sedate soluble phenobarbitone gr 3 intramuscularly may be tried

It is easy to recognise recovery from unconsciousness but difficult in severe cases to assess the gradations that may follow between moderate clouding and full consciousness. In the later stages particularly the patient may appear rational enough on superficial examination or may labour to be allowed up or go home. But until he is fully conscious in the sense that he has insight and memory — correctly orientated and capable of both registering and recalling new information — he should be kept at rest under close observation. Occasionally a post-traumatic psychosis develops — disorientation persisting for days or weeks and being accompanied by a facile mood of euphoria and confabulation. The prognosis however is none the worse for recovery.

In all cases of severe head injury rehabilitation by graduated physical and mental exercises and occupational therapy must be undertaken circumspectly. Allowance must be made for emotional factors which may arise not only from fear of possible harmful consequences but from recognition by the patient of residual disability e.g. dysphasia undue mental fatigue untimely deafness facial scarring or deformities. A nice balance must be maintained between making too hurried or too leisurely progress. The extent to which headache mental fatigue and other symptoms are experienced in response to retraining is a reliable guide. Properly supervised occupational therapy is of special value both in stimulating the recovery of interest in work and in enabling those in charge of the patient to determine to what extent he has regained his original capabilities.

The treatment of post-traumatic epilepsy is discussed in pag 313

For chronic subdural haematoma see pag 301

Subdural hygroma or hydroma due to tearing of the meninges and collection of clear fluid in the subdural space over the vertex or lateral convexity of the brain may produce symptoms indistinguishable from those of chronic subdural haematoma. This lesion may be responsible for persistent headache giddiness and other post-traumatic symptoms

which persist long after consciousness has been fully recovered. The condition is recognised by lumbar encephalography, radiographs being taken immediately and in twenty-four to forty-eight hours after the introduction of air. Treatment is operative.

INTRACRANIAL VASCULAR LESIONS

Subarachnoid Haemorrhage

Absolute rest and quiet are necessary. The use of morphine is justified to relieve agonising headache and pain; its emetic qualities often make it a mixed blessing, but antihistamine drugs such as cyclizine given concurrently will help in this respect. Soluble phenobarbitone gr 1½ 3 intramuscularly is preferable in many cases. In an unconscious patient the routine nursing details must be attended to. Lumbar puncture is an essential diagnostic measure, but the value of repeated thecal drainage is doubtful. Rest in bed should be maintained for six to eight weeks from onset of the bleeding. The patient is allowed to adopt whichever posture is most comfortable and as a rule sedatives such as phenobarbitone are required for several weeks. Return to normal activities must be slow on account of the risk of further bleeding. Hypertensive subjects should have treatment of that condition and straining at stool avoided by the use of laxatives.

Congenital intracranial aneurysm may sometimes be diagnosed before rupture by the advent of migraine of increasing severity, visual defects or oculomotor and trigeminal pareses. Such patients should lead a sheltered life and avoid physical or emotional stress and the surgical possibilities must be considered.

The mortality in the attack phase is up to 50 per cent under medical care and surgical treatment is rapidly becoming routine in young subjects. In suitable cases further haemorrhage is prevented. Hypothermia and hypotensive drugs have made operative interference safer and the present tendency is to operate in about two weeks after cessation of bleeding, although some favour immediate surgery. Cerebral angiography should first be done to determine the presence

and site of the aneurysm and the existence of adequate collateral circulation from the carotid system of the opposite side. Ligation of the internal carotid is successful in young subjects where the aneurysm lies below the level of the anterior clinoid process. Other resources include direct attack on an aneurysm by ligation or clipping. The proximal vessels may be clipped. Ligation of the common carotid artery. Arteriovenous angiomas if small may be excised or have the afferent arteries tied. Large or inaccessible specimens are at present an unsolved problem.

Cerebral Haemorrhage Embolism and Thrombosis

Few elderly hypertensive or arteriosclerotic patients survive intracerebral haemorrhage and little can be done for them. Venesection and the withdrawal of cerebrospinal fluid give no more than temporary improvement. Some cases of cerebral thrombosis and embolism (the latter most frequently encountered as a complication of mitral stenosis) have been treated by stellate ganglion block with procaine. The object being to improve the collateral circulation but there is no proof of the efficacy of this method. Cortisone and other steroids had some vogue in cerebral thrombosis and embolism but there is no convincing evidence of their utility. A. Barham Carter (1957) found anticoagulant therapy valuable in cerebral embolism.

In the apoplectic stage the patient should be nursed in semi-recumbency the head supported on a pillow and the position in bed frequently changed to avoid pressure sores and lessen the risk of hypostatic pneumonia. When there is vomiting it may be desirable to nurse the patient flat with the foot of the bed raised to prevent inhalation pneumonia. The use of antibiotics during the critical first week is to be recommended in hope of lessening chest complications especially in the elderly. Diet may be neglected for a few days but fluid should be given by mouth if the patient can swallow. If not oesophageal intubation is indicated. The mouth should be swabbed free of mucus and saliva at intervals and distension of the bladder avoided by regular catheterisation. A small enema at the outset will clear the lower bowel and prevent soiling of the bed.

In the stage of recovery the paralysed limbs must be put through a full range of passive movement several times daily. Soon the patient will be able to help in performing upper limb movements by interlocking the fingers of the unaffected hand with those of the paralysed limb. Early splinting is undesirable. The paralysed arm should be supported on a soft pillow placed beside the patient. The paralysed lower limb should be kept fully extended at the hip and knee joints and foot drop prevented by a pillow and cradling of the bed clothes. In favourable cases gradual recovery of voluntary power is seen in the leg within a week or two.

Prolonged bed rest is unnecessary and often harmful. As soon as the patient becomes mentally clear and co-operative and signs of recovery are apparent he should sit in a chair by the side of the bed for longer periods each day. The next stage is to support him on either side and encourage standing, part of the body weight being borne by the affected leg. Walking exercises assisted in this way are then begun so that within a relatively short period the patient can manage with one attendant. Meanwhile passive movements of the paralysed arm are given as often as possible, the patient not only adopting the procedure described above but moving the paralysed fingers individually with the aid of his sound hand. In this way the development of spasticity and contractures can be largely prevented and the patient's efforts will be rewarded by the recovery of some voluntary power at the shoulder and elbow joints. Recovery of full voluntary power in the hands and fingers is unusual. But if the general condition of the patient warrants efforts to promote further recovery should be continued long after he is able to walk unaided. When the dominant cerebral hemisphere has been involved with resulting dysphasia the services of a speech therapist are invaluable but discretion must be shown in the selection of patients for clearly not all are likely to profit. Systemic diseases such as hypertension, diabetes and syphilis should receive circumspect treatment.

Cerebral venous thrombosis. May follow mastoid or nasal sinus infection or post partum sepsis. Usually there are repeated Jacksonian or generalised epileptiform fits followed

by hemiparesis. Heparin is recommended with the object of arresting spread of the venous thrombosis but its use is not without risk in puerperal cases. Prompt antibiotic treatment is indicated. Paraldehyde 5 ml should be given intramuscularly at once if there is a succession of fits and this may be repeated if necessary but in most cases the fits cease shortly after their first appearance and with the development of hemiplegia. When there is initial unconsciousness and the period of recovery is slow and marked by noisy delirium, neurosurgical intervention may be advisable to exclude the possibility of an intracranial abscess arising from a septic embolus. A septic embolic source should have appropriate treatment.

Cerebral Hypoxia

A serious complication of cerebral ischaemia which presents in diverse conditions such as severe anaemia, comatose states (hypoglycaemia, barbiturate intoxication and alcoholism), acute respiratory obstruction, hepatic coma, shock and cardiac standstill in the course of general anaesthesia and surgical operations. Early recognition is important as damage due to cerebral oedema is reversible in few.

Treatment consists of securing a free airway (aspiration of pharyngeal secretions and tracheotomy if necessary), oxygen inhalation and mechanically assisted respiration if required, then treatment of the primary factor e.g. anaemia, cardiac failure. Shock and hypotension are indications for supporting the blood pressure by noradrenaline (p. 239). To lessen cerebral oedema, oral fluid is restricted and hypertonic infusions given by vein.

Fifty per cent. sucrose 40 ml and repeat in fifteen and thirty minutes if response not adequate (D. E. Argent *et al* 1956).

Human plasma in four fold concentration

Massive dosage of vitamin B (as Parentrovite)—about 300 mg. thiamine in twenty four hours—is of considerable value.

DISORDERS OF THE EXTRA PYRAMIDAL SYSTEM

Parkinsonism

This syndrome may be the sequel of encephalitis lethargica in young subjects or a manifestation of cerebral arteriosclerosis in the ageing. Parkinsonism in the middle age is usually due to neurotic degeneration of the basal ganglia. Other occasional causes are trauma and cerebral hypoxia e.g. carbon monoxide poisoning.

General management calls for much patience and sympathetic handling. Although intellect is usually unimpaired the condition constitutes a grave barrier to all activities. The sufferer should be encouraged to remain as active as possible to retain previous skills and social and cultural interests. He should be protected from stress and given prompt treatment for intercurrent illnesses. Physiotherapeutic measures are on the whole disappointing but muscle relaxation and postural correction are worth while. The value of psychotherapy is doubtful but the young encephalitic with abnormal personality traits requires prolonged psychiatric supervision if of anti-social proclivities institutional care is necessary.

Drug treatment. Symptomatic improvement is maintained only so long as therapy continues and as tolerance builds up increased dosage or drug combination must usually be employed. Substitution of drugs of different groups will maintain therapeutic effectiveness but the process must be gradual and dosage adjusted to the smallest which controls symptoms.

The *solanaceous alkaloids* (atropine, hyoscyne, stramonium) have a good effect on muscular rigidity and salivation. Tincture of stramonium has the least unpleasant side-effects and dosage is begun with 5 minims three daily before meals and increased gradually to 60-120 minims or more daily. Post-encephalitic subjects display better tolerance than the older degenerative types.

The *synthetic parasympatholytic group* are more effective and less liable to induce unpleasant side-effects than the alkaloids but they have little effect on tremor or sialorrhoea.

Benzhexol (Artane Lederle) caramaphen (Femadrin B.W.) ethopropazine (Parpanit Geigy) procyclidine (Diparcol M & B) and dethazine (Lysivane M & B) are representative Benzhexol is in general use the dosage being 1 mg thrice daily increasing gradually to 10-30 mg daily by divided dosage. Members of these groups must be used with extreme caution in the elderly on account of the risk of precipitating glaucoma.

The *antihistamines and related preparations* are useful in combination or alternation with the above groups. In particular they induce a calm and cheerful state of mind if given towards night sound sleep follows. Diphenhydramine (Benadryl P.D.) phenindamine (Tbephonin Roche) and dimenhydrinate Dramamine Seale are commonly used in parkinsonism. Disipal Camden Chemical has found favour in many clinics for patients resistant or intolerant of the foregoing. Dose 50 mg. thrice daily gradually increased to 100-300 mg. daily. Benztropine Cogentin Merck, Sharp & Dohme (1-3 mg. daily) has affinities with both parasympatholytic and antihistamine drugs and is reputed to be effective against tremor.

Stramonium benzhexol phenindamine is probably the most generally effective popular and pleasant cyclic. Dextro-amphetamine is a useful adjunct particularly to antihistamines. In dosage of 1-3.5 mg. tablets daily it will lighten the mood prevent drowsiness and lassitude and thus inspire activity. It diminishes the severity of oculogyric crises in post-encephalitic subjects.

Surgery Not of general applicability but may be helpful in severe unilateral tremor or rigidity in young subjects. Interruption of the motor tracts at various levels (cerebral cortex peduncle spinal cord) has inherent disadvantages. Section of the efferent fibres of the globus pallidus reduction of its blood supply and alcohol injection have been done for relief of rigidity and tremor without impairment of sensory or motor function.

Hepatolenticular Degeneration Wilson's Disease

Due to an inherited metabolic defect inability to synthesise the copper binding serum protein ceruloplasmin copper

transport is consequently difficult and the metal accumulates in the liver and brain. Osborn and Walshe (1958) demonstrated that penicillamine (β β -dimethyl-cysteine hydrochloride) 0.915 G daily orally has a greater cupruritic effect than BAL. Sodium calciumedetate has also been given to promote copper excretion and potassium sulphide orally diminishes alimentary absorption of copper. Unaffected siblings may require prophylactic treatment.

Chorea (Sydenham & Rheumatic Chores)

Absolute rest in bed in a quiet room or ward is necessary at the outset. If the choreic movements are violent the top and sides of the cot should be padded to prevent bruising and abrasions. A flannel dressing gown should be worn as the bed covers are often kicked off. Food should be liquid or semisolid at first and in severe cases may be given from a feeding cup with a piece of rubber tubing attached to the spout. Choreic children are often undernourished and the caloric intake should be high. liberal protein in the form of milk, eggs and protein supplements is given. When muscular movements and inco-ordination make swallowing difficult feeding should be by tran nasal oesophageal tube of which children are surprisingly tolerant.

Sedatives must be liberally employed at first and phenobarbitone (gr $\frac{1}{4}$ per 14 lb body weight daily) is generally useful. Sodium butobarbitone 0.1-0.2 G twice to three daily may be substituted temporarily in resistant cases. Chloral hydrate in combination with reserpine or chlorpromazine has given good results in severe cases. Aspirin is of definite value where a rheumatic element is conspicuous and is ordered in dosage of gr 30-60 daily with alkalis. The adrenal corticosteroids have also been used in cases showing rheumatic features. their effect on the chorea is doubtful.

When the chorea movements are under reasonable control visits from friends, interesting bed games and activities of an exciting nature may be gradually resumed. Later hydrotherapy and muscle training games lessen awkwardness and hypotonia and have diversional value. Tonics of iron and vitamins are helpful during convalescence. Bed rest should be maintained for a minimum of four weeks in

uncomplicated cases and then the patient may be allowed to sit up in a chair provided that mental poise has been substantially regained. He should be encouraged to rest out of doors when the weather is fine but augmentation of physical activity must be gradual.

Chorea children are usually intelligent and sometimes precocious over pressure of school work and competitive examinations should be discouraged. The domestic atmosphere should be free from extremes of over solicitude and harshness.

After-care is that of other rheumatic diseases. Septic foci such as tonsils should be dealt with on their merits and during a quiescent phase. Routine tonsillectomy is of no value in preventing relapse. Prophylactic chemotherapy appropriate to the rheumatic state may be indicated (see p. 31).

The heredo-familial and degenerative types of chorea require treatment similar to that described for Parkinsonism. Some of these patients ultimately develop psychoses and require institutional treatment.

Chorea gravidarum if mild responds to rest and sedation as described above. Termination of pregnancy will be necessary in severe cases uninfluenced by medical treatment and in those manifesting psychotic tendencies.

The Epilepsies

Anti-convulsive treatment should not be ordered—except as a temporary measure—until the possibility of symptomatic epilepsy has been excluded. When due to syphilis, intracranial tumour, cerebral vascular disease or injury treatment of the primary condition is required. Epilepsy in childhood when related to hypoparathyroidism is effectively controlled by A.T.10 (dihydroxycholesterol). Fits due to hypoglycaemia may be relieved by excision of an islet cell tumour of the pancreas. The occurrence of fits and disturbances of memory in diabetics—especially in elderly subjects—is an indication for reduction or withdrawal of insulin therapy. In temporal lobe epilepsy when a constant discharging focus can be identified, fits may be abolished by excision of the diseased portion of the temporal cortex.

The following recommendations apply to patients suffering from idiopathic epilepsy

General management In a fair proportion of cases regular supervision and anti-convulsive treatment over a period of years will either arrest the fits or reduce their frequency so effectively that the patient can go on with his occupation. The more actively employed a patient is the less the tendency to fits. Occupations involving climbing ladders or contact with machinery are obviously dangerous ■ are swimming cycling driving and sailing. In recent years legislation has made it possible in some districts for a proportion of epileptics to be employed in groups on approved work in factories. The importance of steady employment and interest in the job cannot be exaggerated.

The education of child epileptics must be encouraged. Serious cases with mental defect or antisocial tendencies are best treated in special institutions.

Over indulgence and excesses of all kinds are harmful and alcohol should be avoided also the drinking of large amounts of fluid—a practice which may induce attacks. The potential danger of taking long journeys without food and of irregular meals should also be mentioned but apart from these reservations the patient should be encouraged to lead as natural a life as possible. Dietetic restrictions are unnecessary although a ketogenic diet ■ occasionally useful to tide a child over a particularly severe convulsive sequence.

Drugs Once begun treatment should be continued without intermission until the patient has been free of fits for three years. The irregular use of anticonvulsant drugs is ineffectual and dangerous on account of the risk of status epilepticus. If fits occur only infrequently careful consideration should be given as to whether drugs are really necessary or expedient and if the patient is not prepared to take them steadily he is probably better without.

All patients should be seen regularly e ■ fortnightly or monthly at first and then at increasing intervals depending on the fit frequency. If for any reason it ■ desired to change a drug it should not be withdrawn suddenly but gradually replaced by the new one.

Bromides are rarely used not because they are ineffectual

but because slightly better results are obtained with phenobarbitone and newer drugs which are taken as solids. They are useless in psychomotor and petit mal epilepsy. Their tendency to cause skin rashes and digestive disturbances can be corrected to some extent by the addition of alkalis or small doses of Fowler's solution. The usual dose is gr 30-60 (2-4 G) daily for an adult. Good effects are dependent on maintenance of the blood bromide level at about 200 mg per cent. Tincture of belladonna or sodium borotartrate (gr 10-15 thrice daily) may be given in combination with bromides and smaller doses will then suffice. If the fits show diurnal or nocturnal incidence the major proportion of the daily dose should be taken about an hour before the anticipated time of onset. If the attacks synchronise with the menses the dose of bromide (or other antileptic agent) should be doubled during the few days before the period and halved in the intermenstrual phase: salt and fluid restriction and diuretics may also help.

Phenobarbitone is the most popular remedy for major epilepsy. It may be used alone or in combination with bromides or phenytoin. Phenobarbitone is given in dosage of gr 1-4 daily divided according to the main incidence of the attacks. Combined therapy is often more successful than larger doses of a single drug. For mainly diurnal fits gr 12 of phenobarbitone should be taken on rising and gr 15 of bromide on retiring. The smallest dosage which controls the attacks is the correct one: overdosage with barbiturates may increase attack frequency. As a rule phenobarbitone gives rise to no unpleasant side-effects. Somnolence may occur at the upper dose levels but this can be counteracted by the administration of caffeine citrate gr 5 or amphetamine 5 mg daily. Urticarial and morbiliform rashes occasionally occur. Methylphenobarbitone (Romunal, Bayer) is much less sedative in action, and is used in double the phenobarbitone dosage.

Primidone ('Mysoline', I.C.I.) is claimed to be less toxic and more effective than the foregoing in controlling grand mal. It is useful against psychomotor and focal attacks also.

The initial dose is 0.25 G daily for three days, this being increased to a total of 1.5 G daily in divided fractions.

Children show relatively good tolerance initial dose 0.125 G increased in the same way

Soluble phenytoin (Epanutin P.D. Solantoin Glaxo) Effective in many cases of grand mal and it benefits a proportion of petit mal sufferers. Its hypnotic action is slight, the main action being elevation of the convulsive threshold. The dose is 0.2-0.6 G daily and the capsules should be given with two ounces of water after meals. This drug may convert grand mal attacks to the petit mal pattern but it has a good effect in psychomotor attacks which are uninfluenced by barbiturates. Phenytoin is very frequently used in conjunction with barbiturate therapy particularly in mixed epilepsy and the adult requirement is in the region of gr. 4 of each.

Toxic manifestations are commoner than with the above-mentioned drugs and consist of mental irritability and confusion, skin rashes, ataxia and gingival hyperplasia.

In cases not adequately controlled by phenobarbitone phenytoin therapy methoin (Mesantoin Sandoz) may be given alone (0.1 G thrice daily and slowly increased) or added in (0.1 G daily and increased by 0.1 G weekly). Blood dyscrasia may complicate methoin treatment. Megalocytic anaemia may complicate treatment with phenobarbitone, primidone and phenytoin. Folic acid has been found effective in correction of anaemia and reduction of fit incidence.

Troxidone (Tridione Abbott) Exhibits a reverse action to other anti-epileptic drugs in that it is more effective against petit mal and its myoclonic and akinetic variants than grand mal. Its efficiency in controlling petit mal however is by no means constant and toxic effects are common in the shape of dermatitis, nephrosis, hepatitis, aplastic anaemia and thrombocytopenic purpura. Careful supervision is required therefore of all patients taking the drug and it should not be prescribed in the presence of renal or hepatic defect. It is supplied in 0.15 G capsules and the daily adult dose is 3-7 capsules, infant 1 capsule, two to four years 2 capsules, five years 3 capsules.

In cases of mixed grand and petit mal troxidone must be given in combination with phenobarbitone or phenytoin to control the convulsive element.

Phenacemid (Miloptin F.D.) Possesses marked anti convulsant properties with little toxicity should be tried in cases resistant to trovdone. Dose 1-2 capsules of 0.5 G (twice or thrice daily (infants 0.5 G daily) Withdrawal must be gradual. The most effective remedy for petit mal and pyknolepsy. Not advised in pure grand mal.

Acta olamide (Diamox, Lederle) A carbonic anhydrase inhibitor diuretic which acts by reducing pH of the blood thus raising the convulsive threshold. It is worth trial in premenstrual epilepsy.

Treatment of the attack. If heralded by subjective phenomena e.g. tingling in an extremity prompt application of a tourniquet may check the fit. In cases with prolonged aura, a powerful muscular effort or an inhalation of amyl nitrite may act similarly. During the seizure the patient should be laid recumbent with the head turned to one side and tight clothing and neckwear loosened. A rubber wedge or a padded key should be inserted between the jaws to prevent injury to the tongue. Frothy mucus, blood or vomitus must be wiped from the mouth. Gentle restraint may be used to prevent the patient from injuring himself against hard objects. He should be allowed to remain quiet for some time after the convulsions have subsided.

Status epilepticus. A serious condition characterised by a succession of convulsive seizures without conscious intervals. Soluble phenobarbitone gr. 1 intramuscularly is a useful drug and the dose may be repeated in three hours. Thiopentone sodium (Pentothal, Abbott) is used intravenously also. Bromethol (Verurin, Bayer) in dosage of 0.1 ml. of 2.5 per cent. solution per kg. body weight rectally after a cleansing enema is used in obstinate cases. Paraldehyde is the safest and most satisfactory routine. 8-10 ml. is injected into the gluteal muscle with massage of the injection site. Subsequently 5 ml. is injected every half hour until the fits cease. The paraldehyde can if necessary be added to an intravenous drip.

Migraine

Heredity and constitution play an important part, the headaches tending to recur at irregular intervals and with

soothing food is regarded with extreme distaste but glucose drinks and strong coffee should be given. One or other of the following analgesics may be prescribed soluble aspirin or codeine compound tablet gr 10-20 Tabloid Empirin Compound with Codeine BW one to two tablets and repeat in two hours if necessary Nembudene Tablets, Abbott similar dosage

Ergotamine tartrate is most effective in relieving migraine by reducing the amplitude of arterial pulsations and restoring vascular tone 0.25 mg is given subcutaneously and if only partially successful may be repeated in six to twelve hours In subsequent attacks an initial dose of 0.5 mg may be used if necessary but the maximum is 1 mg in twenty four hours Oral combinations based on ergotamine are popular for episodic therapy (Migrit BW Orgraine Organon) Dose up to 6 tablets over 4 hours Prochlorperazine (Stemetil M & B) is effective for relief of nausea and vomiting Prevention 20 mg daily cure 20 mg followed if necessary by 10 mg in one hour

Headache

Every effort must be made to find the cause of the headache before relegating the sufferer to symptomatic treatment The best routine drug is aspirin alone or in combination with codeine caffeine or phenobarbitone Refractive error nasal sinus disease and histamine sensitivity are occasionally responsible headaches may be due to industrial toxic factors or unhygienic working conditions while a large proportion are of psychogenic origin Their importance lies in the prolonged disability to which they may give rise and the useless expenditure of drugs which may be occasioned by failure to recognize this cause Psychotherapy may be curative after a few interviews Cases showing fibrositis of the posterior cervical muscles respond to infiltration of the trigger spots with procaine and stretching the affected muscles Dietetic indiscretions dyspepsia biliousness and constipation are often blamed for headache occasionally the removal of impacted faeces from the rectum gives dramatic relief In dyspeptics addicted to the use of alkalis however headache and vomiting may be signs of alkalosis and prompt

relief follows stopping these drugs. Chronic microcytic anemia in women is often overlooked as a cause and iron therapy is curative. The treatment of headache and vomiting in arterial hypertension is described in page 238.

Anorexia Nervosa

This is a psychogenic disorder and found mostly in young women. Complete failure of appetite quickly follows refusal of food and a serious state of emaciation and inanition supervenes. Absence of wasting of the breasts and external genitals and retention of axillary and downy hair are characteristic. Treatment is by psychotherapy planned in accordance with the patient's environment and difficulties. Progress is likely to be hindered by the ministrations of harassed and solicitous relatives and removal of the patient to hospital is desirable. A capable nurse of strong personality can usually persuade the sufferer to eat. Insulin therapy and prefrontal leucotomy have been used.

Tics and Habit Spasms

An unstable or over-sensitive nervous system is often associated with such conditions but many ticquers being otherwise well adjusted are successful in life and paying no attention to their tic suffer little or no embarrassment from them.

In children all sources of peripheral irritation should be attended to e.g. uncomfortable clothing (shrugging tics) visual defects (blinking tics) nasal catarrh (sniffing tics). The general health should be improved by adequate outdoor exercise and nourishing diet. Care must be taken however not to overdo such treatment as harm may be done in focusing undue attention on the complaint. Domestic or school anxiety injudiciously handled by parents or teachers is a common cause of tic in school children and psychotherapy is often needed. The aim is to restore the child's confidence and persuade the parents to ignore the tic. When this cannot be done at home there is much to be said in favour of bringing the child into hospital for a short period of supervision and mild sedation.

Spasmodic torticollis. This rare complaint of adults may follow mental shock or occasionally *encephalitis lethargica*. In most cases the ætiology is obscure and treatment disappointing. When the condition is hysterical dramatic results may follow treatment by suggestion or hypnosis but in true spasmodic torticollis it cannot be said that psychotherapy has any curative effect although it may help the patient to adjust himself to the disability.

In recent cases with severe involuntary movements rest in bed for three or four weeks is indicated and phenobarbitone or bromide in small doses should be given. If there is improvement the patient may then be encouraged to carry out remedial exercises in front of a mirror. Possible contributory causes—errors of refraction and osteoarthritic changes in the cervical spine—should be sought and treated. Splinting by means of a plastic or metal collar may be tried when the movements are not severe and can be checked by the patient supporting the chin with his hand. But usually such mechanical devices fail to achieve their purpose. The same applies to operative treatment (division of nerves or muscle fibre) which has had extensive trial in the past. Temporary relief may follow but the movements tend to recur or spread to neighbouring groups of muscles.

THE CRANIAL NERVES

Optic Nerve

Papilloedema due to increased intracranial pressure is an indication for operative relief to avoid blindness. In all cases of apparent primary optic atrophy the possibility of a local lesion—chromophobe adenoma or suprasellar cyst, meningioma, congenital aneurysm, arachnoiditis—should receive consideration before the condition is assumed to be irremediable. Sudden blindness preceded by distressing facial pain may occur in the elderly as a consequence of temporal arteritis. If the optic atrophy is due to syphilis or poisoning by metals, benzene ring derivatives, alcohol or tobacco, therapy appropriate to these conditions must be instituted. Retrobulbar neuritis may be due to disseminated

sclerosis gross dietary and vitamin deficiency syphilis or disease of adjoining structures and treatment of the primary condition is indicated Thiamine and cortisone have given good results in some cases

Oculomotor Nerves

Lesions may be caused by injury or disease of the brain stem or by raised intracranial pressure and treatment must be directed to the main condition Diplopia and ptosis are sometimes the first signs of myasthenia gravis (p 306) Unilateral sixth nerve palsy may occur as a sequel of spinal anaesthesia The wearing of an eye shade or of spectacles having a frosted glass covering the affected eye obviates diplopia and vertigo Ptosis may be relieved by plastic procedures Ocular deviation is sometimes improved by operation provided that the lesion has become stationary Prisms are of little help

Trigeminal Neuralgia

Infective conditions of the teeth and nasal sinuses call for treatment Symptomatic relief may be given by aspirin phenacetin and codeine Quinine may be combined with aspirin and codine in powder form Local treatment with rubefacients and short wave diathermy gives temporary relief in some cases

Lost herpetic neuralgia can be so persistent and intractable in elderly subjects as to lead to depression and suicidal intent Deep x ray treatment to the region of the Gasserian ganglion on the affected side is sometimes effective but alcohol injection or section of the sensory root is of little avail It may be justifiable in certain cases to recommend the operation of leucotomy

The *douloureux* is distinguished by its paroxysmal quality localisation of the pain to one or more divisions of the nerve presence of trigger points absence of any sensory impairment and freedom from pain between attacks Usually the cause is not obvious medicinal treatment fails and pethidine or the inhalation of nitre is required to bring relief Treatment by alcohol injection is effective the injection being given into one or other branch of the ganglion

Injection of the ganglion is to be preferred in elderly debilitated subjects who are unsuitable for the more formidable procedure of retroganglionic root section. The sensory loss which follows successful treatment may cause troublesome keratitis if an eye shield is not used. The conjunctival sac should be irrigated for some weeks after operation.

Temporo-mandibular neuralgia (Costen's syndrome) This is responsible for a number of cases of atypical facial neuralgia. The pain is noticed especially on chewing and is referred to the ear and the side of the tongue. There is often a history of forcible opening of the jaws through inserting a gag at operation or of dental clearance, the dentures fitting badly and allowing overclosure to occur on biting. Temporary relief from pain can be had by the injection of procaine into the petrotympanic fissure, but good results are obtained in edentulous subjects by providing a specially built up lower denture to prevent overclosure of the bite.

Glossopharyngeal neuralgia This may arise independently or as a complication of tonsillar or pharyngeal neoplasm or inflammation. The medical treatment of idiopathic cases is as for trigeminal neuralgia. If ineffective, section of the nerve in its intracranial course may be done.

Facial Nerve

The nerve may be involved in lesions in the cerebello-pontine angle (rarely acoustic neuroma), in the temporal bone (otitis media) or in its external course (trauma). Facial palsy may be an early sign of polyneuritis and it occurs as an isolated symptom occasionally in disseminated sclerosis. In these conditions treatment of the primary cause is indicated.

The most common variety—Bell's palsy—is attributed to compression or neuritis in the aqueduct or trauma in its external course. Spontaneous recovery is to be expected in the majority of cases within weeks or months. Protection of the affected side of the face is necessary and for the first week the patient should stay indoors, preferably resting. Thereafter exposure to wind and dust should be avoided and an eye shade worn. Undue stretching of the paralysed muscles should be prevented by wearing a light splint. *g*

a piece of bent copper wire covered by cycle valve tubing the appliance being moulded to the side of the face with one end hooked into the corner of the mouth to retract it and the other held in position behind the auricle. Active movements before a mirror are helpful.

It is advisable two or three weeks after the onset to test the electrical reactions of the paralysed muscles. A normal response indicates the probability of repair and complete recovery. Absence of any response to faradism is a sign that recovery may be slow or incomplete. In these circumstances there is justification for the employment of massage and gentle galvanic stimulation. If there is no sign of recovery however it is unwise to persist with the latter as unsightly contractures may result. Diathermy may be tried empirically but vitamins and drugs internally are useless. Occasional successes have followed cortisone therapy. Decompression operations have been successful in selected chronic cases (T. Cawthorne 1936). Facial slips and nerve grafting have been employed to diminish the facial disfigurement in irrecoverable cases.

Facial hemispasm. Reassurance that the condition is not likely to progress may be given in most cases. Nervous subjects benefit from small doses of phenobarbitone. Injection of the facial nerve with alcohol is rarely justifiable and it will be undertaken only after its effects in causing paralysis have been fully explained.

Auditory Nerve

Tinnitus may be the result of wax in the auditory meatus, middle ear inflammation or otosclerosis. It occurs in Ménière's syndrome, in acoustic neuroma, arterial hypertension, after fractures involving the temporal bone and in temporo-mandibular neuralgia. Treatment is of the underlying cause. When the cause is not apparent and the tinnitus is accompanied by signs of anxiety or depression a difficult decision arises—whether to recommend such a radical procedure as labyrinthectomy or intracranial division of the nerve or to treat the case as a psychiatric problem. Sedatives such as phenobarbitone gr $\frac{1}{2}$ twice daily (with or without reserpine or chlorpromazine) may be tried, but if the affective

disturbance grows along with obsessional preoccupation with the symptom and no physical cause can be found electrical convulsion therapy may be indicated

Ménière's syndrome The patient should lie quiet until the attack subsides. An inhalation of amyl nitrite will help in hypertensive cases. For severe attacks ■ subcutaneous injection of morphine or an intravenous dose of soluble thiopentone may be necessary

Phenobarbitone is the best prophylactic remedy. Dehydration therapy (low sodium diet ammonium chloride and fluid restriction) ■ occasionally of service (6-9 G ammonium chloride daily in 0.5 G enteric-coated tablets)

Histamine desensitisation has been used for relief of this troublesome syndrome. The improvement may be due in part to vasodilatation. For non reactors to histamine nicotinic acid may be tried in dosage sufficient to cause flushing of the face (50-100 mg thrice daily by mouth for four to five weeks) followed by smaller maintenance dosage. This ■ useful for postural vertigo occurring independently of the labyrinthine seizures. Antihistamines such ■■ dimenhydrinate Dramamine Searle (50 mg thrice daily) cyclizine Marzine BW (in similar dosage) suit some patients for interval treatment while others benefit from chlorpromazine Largactil M & B 25 mg twice daily or its analogue prochlorperazine Stemetil M & ■ 5-10 mg twice daily

If all medical measures fail as ■ the case in 10 per cent of patients treated section of the eighth nerve (or destructive labyrinthotomy) should be considered. Severe but temporary vertigo follows but a considerable degree of compensation ultimately occurs in the orienting mechanism. Cervico dorsal sympathectomy is good in unilateral affections it relieves vertigo and preserves hearing

Motion sickness Hyoscine hydrobromide ■ a good remedy and gr $\frac{1}{160}$ should be given orally one hour before embarkation and repeated in two hours. Further doses at six hourly intervals for twenty four hours if necessary

Antihistamine drugs have a prophylactic and curative action in motion sickness. Gay and Carliner report good results from oral or rectal dosage with dimenhydrinate

Dramamine Searle a substituted derivative of diphenhydramine Prophylactic dose is 50 mg four hourly and before retiring for the first forty-eight hours of the voyage Curative dosage is about double this amount If necessary the tablets may be suspended in saline and given rectally

Cycline (Marzine B.W.) causes less drowsiness One 50 mg. tablet should be taken thirty minutes before embarkation and repeated four hourly for forty-eight hours if necessary

Hiccough Hiccough is a troublesome symptom which may have such diverse causes as epidemic encephalitis tabetic crises pericardial effusion and uremia In simple irritative cases holding the breath for as long as possible may cure The same result may be obtained by making the patient breathe into a paper bag Irritation of the nasal mucosa until sneezing is provoked a mouthful of iced water or a dose of undiluted spirits or Worcester sauce is effective on occasion

If the hiccough is symptomatic of a serious malady appropriate treatment should be initiated this includes such fundamentals as relief of abdominal distention or diaphragmatic irritation and correction of metabolic abnormalities Sedatives such as phenobarbitone chloral or hyoscine may be necessary Neuritic and toxic types benefit from the intravenous administration of glucose saline solution with 25-50 mg chlorpromazine (Largactil M & B) Further dosage with chlorpromazine (25 mg by mouth or vein) may be given as required

deformities. In quiescent joints expert movement will often restore useful function and remedial exercises are planned with the object of retaining the improved function. Arthrodesis of the knee elbow arthroplasty amputation of toes and excision of the ulnar head with radio-carpal arthrodesis have definite scope in correcting deformity or improving function when the active inflammatory phase has passed.

Ankylosing Spondylitis

The general treatment outlined for rheumatoid arthritis is valid. Gold therapy is often useless. Cortisone is helpful in management of acute exacerbations and phenylbutazone is an effective analgesic. Chloroquine is of some value. Soft tissue relaxation is promoted by prolonged rest in the supine position. The bed should be firm and fracture boards inserted to prevent sagging. Pillows should be dispensed with as the spine straightens and this process is hastened if a long narrow pillow is placed longitudinally under the spinal column. The application of a Savre's traction sling to the patient's neck will extend the cervical spine and assist in recovering its mobility. Guthrie Smith's method of spinal slinging is useful for correcting kyphotic deformity. Serial plaster casts or a hinged cast may be applied for correction of spinal flexion and later a spinal brace of the Goldthwaite type will help to maintain orthopaedic improvement. Massage to the back muscles will improve tone and relieve spasm.

Re-educational exercises should be prescribed to correct postural deficiencies to strengthen the shoulder girdle muscles and to overcome costo-vertebral fixation which increases the incidence of upper respiratory infections. Deep x ray therapy is indicated in all cases. It has been shown that the incidence of leukaemia in patients so treated is about 2.5 per cent i.e. the risk of acquiring the disease is increased ten fold. This however does not weigh heavily against the method.

A corrective osteotomy may be desirable for severe fixed flexion deformity.

Osteoarthritis

The general health should receive attention and occupational trauma of the affected joints avoided. Obese

patients do better when suitable reduction measures are put in train. Metabolic or endocrine abnormalities *e.g.* diabetes, hypothyroidism, menopausal upset must be treated. Elimination of local sepsis is desirable on general principles although the course of the disease is rarely influenced thereby. Since osteoarthritis is degenerative rather than inflammatory in nature cortisone and dectasteroids are unlikely to have a striking suppressive rôle but in early cases these hormones relieve pain and enhance the efficacy of other measures. Intra articular injections of hydrocortisone are of some value in early cases. Aspirin, phenacetin and codeine are necessary for relief of pain. Gold treatment is of no avail in osteoarthritis.

A judicious admixture of rest, exercise and physiotherapy will help to conserve useful and painless function. During exacerbations of the disease affected joints should be placed at rest by splinting or traction. Heat in the form of electric pads or short wave diathermy is soothing and a full range of passive movements should be executed daily. More active physiotherapy may be instituted as soon as the patient is free from pain and the objectives are to delay loss of joint function and correct postural deformities. Improvement in tone of the relative muscle groups is the most important rôle of physiotherapy. Diathermy, infra red and wax bath treatments relax spasm and make other manipulations more effective. Massage to the muscles and passive and active movements are then given followed by postural exercises. These remedial movements can with great advantage be done in a pool bath.

Deep x ray therapy is useful where pain is a feature or where the joint lesions are rapidly progressive.

Orthopaedic treatment is helpful at all stages of the malady. Provision of support, fixation or prevention of weight bearing by means of suitable apparatus will keep the patient active and comfortable.

Operative measures should be considered for extensive involvement of major joints. Removal of the patella and removal of bony spurs and synovia are sometimes helpful in knee joint affection. Arthroplasty of the hip joint has not proved uniformly successful but the Schanz type of

subtrochanteric osteotomy with excision of osteophytes restores useful hip flexion. Obturator nerve section is occasionally done to relieve hip joint pain in elderly and feeble subjects.

Osteoarthritic Spondylitis

Treatment in general as for the rheumatoid type. Defective posture should be corrected by traction-extension or plaster collar or jacket. Physiotherapy is useful for improving posture and muscular tone. Radiotherapy is beneficial in early cases. Operative treatment is occasionally symptomatic or for fusion in cases showing disorganisation of required in localised spondylitis either for relief of pressure intervertebral articulations.

Fibrositis

The commonest form of non-articular rheumatism usually affecting the cervical shoulder girdle and lumbar muscles. Various localisations attract specific nomenclature e.g. lumbago, myofascial sciatica, multifidus triangle syndrome, intercostal myalgia.

The influence of cold, damp and muscular overstrain is considerable and these should be avoided. Ill-fitting and draughty driving seats of motor vehicles and the closing of unwieldy garage doors are common precipitating factors. Some cases show a background of neurosis. Care must be taken to exclude serious conditions like ankylosing spondylitis, intervertebral disc lesion, myelomatosis or other neoplastic involvement of spine or pelvis.

In the simplest forms rest to the affected region and the application of heat by kaolin poultices, hot stupes or baths, electric pad or short wave diathermy will produce prompt relief.

More extensive cases require rest in bed and continuous warmth. The presence of systemic disease should be excluded and in the case of lumbar or gluteal fibrositis abnormality of the spine, pelvis and pelvic viscera should be sought for. Focal sepsis in teeth, tonsils, gall bladder or prostate may perpetuate fibrositic manifestations and appropriate treatment is desirable. Salicylates and iodine may

be given also analgesic preparations as required. Physio-therapeutic measures include deep massage to the affected muscles and movements designed to stretch them. The use of hot pool baths increases the patient's tolerance of these measures. Injection of local anesthetic solution into tender points or trigger spots pressure on which elicits radiating or referred pain is a valuable method of treatment as it provides a pain free interval in which manipulation and full movement of the affected muscles may be performed thus relieving adhesions. H. A. Burt (1957) recommends 5-10 ml of 0.5 per cent Lignocaine Hydrochloride B.P.C. with 25-50 mg hydrocortisone and an ampoule of hyaluronidase (Hyalase Benger).

CHAPTER XVII

TROPICAL DISEASES

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Malaria

Malarial infection can be variously acquired 1 Commonly by the bite of an infective female anopheline mosquito in an endemic area 2 By transfusion of infected blood 3 By inoculation either accidental or intentional as a therapeutic measure in paralytic dementia 4 Malaria may occur in the newborn probably by transference of parasites from the maternal blood through placental injury during birth

Malarial infection may be overt or give rise to ill-defined relapses with chronic malaise and anaemia It should be noted that at the inauguration of a primary attack the fever remains continuous for some days and the characteristic recurrent pyrexia does not appear until schizogony has developed its proper rhythm This point may help to distinguish a fresh infection from a relapse

Treatment The choice of drug depends on (1) The degree of acquired immunity (2) The species of the parasite (3) The object to be attained *e.g.* whether treatment of an acute attack or eradication of the exo-erythrocytic phase

Treatment of a clinical attack (a) *Non Immune subject* In *P. falciparum* infections there must be no delay in starting antimalarial treatment (danger of cerebral malaria) One of the 4 aminoquinolines chloroquine (Aralen Bayer Nivaquine M & H) or amodiaquine (Camoquin P D) should be used Each tablet contains 0.15 g chloroquine base The

dose is 4 tablets initially followed by 2 tablets in six hours then 2 tablets daily for two days. Each tablet of amodiaquine contains 0.2 G of base and the dose is 3 tablets initially and 2 daily for two more days. Mepacrine hydrochloride 0.9 G on the first day 0.6 G on the second day and then 0.3 G daily for five days may also be used. Quinine is now seldom ordered as it may induce intravascular hæmolysis (black water fever).

In severe cases oral treatment may be too slow and parenteral therapy is required. (i) chloroquine hydrochloride 0.2 G intravenously and repeated in six hours if necessary. Or (ii) mepacrine methane sulphonate 0.375 G intramuscularly repeated in six hours. Or (iii) quinine dihydrochloride 0.65 G (gr. 10) in sterile normal saline injected slowly (not more than gr. 1 per minute). Three such injections may be given in a twenty four hour period.

(b) *Subjects partially immune*. A single oral dose of one of the above drugs is usually sufficient. Thus either chloroquine 0.6 G (4 tablets) amodiaquine 0.6 G (3 tablets) or mepacrine hydrochloride 0.3-0.5 G should be given in one dose.

Cure of relapsing malaria. Relapses in *P. vivax* and *P. malaria* infections are due to persistence of the trophozoitic phase. This may be eradicated by the administration of one of the 8 aminoquinoline compounds. Of this group primaquine and pamaquin are the drugs of choice. The dose of primaquine is 15 mg. daily for fourteen days. Careful supervision is necessary because of the occasional unpredictable occurrence of acute intravascular hæmolysis. Treatment with these drugs should be combined with an ordinary therapeutic course of chloroquine or amodiaquine but not mepacrine. Proguanil (Paludrine) and pyrimethamine may also be useful in eradicating malignant tertian infections but their action is slow. They are best reserved for prophylaxis.

Prophylaxis and suppression. In order to obtain the full effect of any drug, regular dosage is essential. Chloroquine 0.3 G (base) or amodiaquine 0.4 G (base) weekly are effective suppressants. Mepacrine taken over long periods may produce a lichenoid dermatitis, and does not appear to be any more efficient than chloroquine or amodiaquine.

Proguanil monohydrochloride 100 mg daily or pyrimethamine 25 mg weekly have the advantage of acting on the pre-erythrocytic as well as the asexual erythrocytic forms of the parasite. Drug resistance may appear in areas where either of these compounds is in common use.

Management of common malarial conditions 1 *An ordinary attack of ague* Confine to bed and give copious fluids e.g. lemonade, broth. Keep the patient warm during the chill stage and change the bed coverings frequently in the sweating stage. Iced water compresses are useful for relief of headache. A standard drug treatment should be instituted at once. The patient may be allowed up after a few days' freedom from fever, but he should avoid chill and fatigue during convalescence. Iron should be given for two weeks or longer if the hæmoglobin is low.

2 *Bilious remittent fever* This condition should be clearly differentiated from blackwater fever by examination of the urine. Give fluid diet with extra glucose. For vomiting sips of iced water and heat to the epigastrium. Institute a standard drug treatment. If vomiting interferes with oral administration of antimalarial drugs the intravenous route must be substituted. Convalescence should be prolonged and anaemia corrected by iron.

3 *Cerebral malaria* A disease of protean manifestations and in tropical practice its presence should be suspected in any patient showing pyrexia, heat effects, unusual neurological signs or mental symptoms. It frequently arises in new arrivals to the tropics (incidental malaria).

Intravenous chloroquine should be given on suspicion and the patient treated as for heat hyperpyrexia (See p. 73). When consciousness returns a standard course of oral treatment is begun. At least one month's rest in a healthy climate is necessary before returning to work.

4 *Blackwater fever* Some areas of malarious countries are notorious for the incidence of this extremely serious condition. Such are usually hyperendemic with spleen rates of over 50 per cent. Blackwater fever is a recurrent disease and the prognosis worsens with each relapse. The onset is heralded by nausea and vomiting with rapid development of intense jaundice and passage of port coloured urine.

The following routine must be established immediately

- 1 Stop all anti malarial drugs
- 2 Do not attempt to transport the patient a long distance to hospital. Absolute rest in bed is essential
- 3 Maintain fluid and electrolyte balance. If anuria develops institute treatment described on page 194
- 4 A blood transfusion should be given if available and repeated daily if anaemia is severe. The blood must be carefully matched
- 5 ACTH and cortisone have been shown to exert a beneficial effect on the haemolysis
- 6 Antimalarial treatment avoiding quinine can be safely given during the comatose period

African Trypanosomiasis

The disease is due to infection with trypanosomidae transmitted by bites of tsetse flies. 1 *Trypanosoma gambiense* vectors: *Glossina palpalis* and *Glossina fuscipes*. 2 *Trypanosoma brucei* vectors: *Glossina morsitans* and *Glossina swynnertonii*. Trypanosomiasis is common in animals thus creating a reservoir of infection.

The incubation period is from seven days to three weeks. Occasionally an infected person may show no symptoms for many years. The second stage is characterised by pyrexia, erythema, splenomegaly and superficial lymph gland enlargement, most prominent in the posterior cervical triangle. The terminal stage is marked by mental deterioration with delusions, mania and characteristic lethargy. The disease is most amenable to treatment during the first and second stages.

Treatment 1 *Trypanosomae*. Effective at all stages, and specially indicated in the cerebral stage. The initial dose is 1 G intravenously or intramuscularly and this may be gradually increased to 3 G in subsequent injections at seven day intervals. The amount necessary for maximum therapeutic effect is 24 G. Trypanosomes readily become resistant. Toxic effects are (a) Primary optic atrophy. Treatment consists of cessation of arsenical therapy and intravenous

administration of sodium thiosulphate (Ametox M & B 10 per cent solution) 0.5 l □ twice daily (b) Exfoliative dermatitis BAL is a useful remedy for this complication

2. *Mel B (Arsobal)* a combination of melarsen with dimercaprol a potent trypanocide especially useful in tryparsamide resistant subjects. Many early cases have been cured by a single dose but a course of three daily injections of 0.2 G intravenously is commonly used. Purpura and albuminuria may be caused by this drug and it should therefore be used only in hospital. May & Baker produce a standardised product of Mel B in 5 ml ampoules containing a 3.6 per cent solution in propylene glycol. A preliminary test dose of 0.5 ml of this solution should be given before embarking on one or several courses of treatment.

3. *Suramin (Bayer 205 Antypol)* Given in dosage of 1 G in 10 ml of water intravenously. In early cases 5 G given over one week will produce maximal therapeutic effect but the course should be continued until 10 G has been given. This drug has certain disadvantages (a) It may cause renal damage urticarial or herpetiform eruptions (b) It is useless in the cerebral stage of the disease.

4. *Pentamidine (M & B 800 ; diamidino diphenoxypentane)* Given in daily intravenous doses of 100 mg in 10 ml of distilled water for twelve days. Toxic effects are nausea vomiting pruritis and fall in blood pressure.

Courses of drug treatment 1 Early cases First and second stages of the disease Suramin 1 G intravenously weekly for ten weeks or one dose of 1 G intravenously followed by tryparsamide 1.2 G at intervals of five days for nine to twelve doses or pentamidine 100 mg intravenously daily for twelve doses.

2. Late cases with cerebral involvement suramin 5 G intravenously over one week. One week's rest interval. Then tryparsamide 1 G increasing to 3 G twice weekly to a total of 24 G. Mel B should be used in tryparsamide resistant cases.

Prevention 1 Isolation and adequate treatment of all infected persons. 2 The destruction of tsetse flies and their breeding places in settlements and individual precautions against bites. 3 Prophylactic treatment of exposed persons with 1 G of suramin at intervals of three months.

Leishmaniasis

This term includes two conditions due to infection by flagellate protozoa of the genus *Leishmania* kala-azar caused by *Leishmania donovani* and oriental sore due to *Leishmania tropica*. The organism is readily obtainable in stained films of blood, sternal marrow and spleen juice. It is transmitted by the bite of the sandfly *Phlebotomus*.

Kala-azar Visceral Leishmaniasis

World wide distribution \equiv India, China and the Mediterranean littoral. There is a characteristic continuous pyrexia with a double rise each twenty four hours. Epistaxis and pigmentation of the face are early signs. Leucopenia with progressive enlargement of the liver and spleen follow.

Treatment *Sodium stibogluconate* Pentostam B.W. A stable solution containing the equivalent of 100 mg penta val antimony per ml. for intravenous or intramuscular administration. Begin with small doses (1-2 ml) and gradually increase the dose on alternate days to 6 ml. 60 ml. constitutes a course and the drug is well tolerated.

Neostam B.W. prepared as a 4 per cent solution in distilled water 0.1 G. per 100 lb. body weight is given slowly intravenously on alternate days to a total of 3 G. per 100 lb. body weight.

Urea stibamine A useful preparation and free from side effects if given intravenously initial dose 0.1 G. second dose 0.2 G. subsequent doses 0.25 G. Fifteen daily injections should be given. this course may be repeated after one month if necessary.

Tartar emetic A freshly prepared 2 per cent solution in distilled water \equiv injected intravenously commencing with 2 ml. Subsequent alternate daily doses are increased by 1 ml. to a maximum of 5 ml. A course consists of 4 G.

Lithium antimony thiomalate (Anthiomaline M & B) Prepared as a 6 per cent solution 1 ml. containing the equivalent of 0.01 G. antimony. This drug gives good results by the intramuscular route and is particularly useful for children. Commence with 0.5 ml. and increase by this amount on alternate days until 2.5 ml. is being given. Continue with this dosage for a total of twenty injections.

The pentavalent compounds mentioned above have displaced the *invalents* e.g. *Tartar emetic Anthiomaline* from favour

Stibamidine Useful for cases resistant to other drugs. The solution should be freshly prepared and administered slowly into a vein. The dose is 1 mg. per kg. body weight and the amount necessary for cure is about 400 mg. Subjective disturbances over the ingeminal area frequently arise during treatment. More recently hydroxystibamide has been used 3.3 mg. per kg. intramuscularly each day for ten to twenty days.

General management of a case of kala azar. Attend to any concurrent condition such as malaria, ankylostomiasis or anaemia. Blood transfusions may be necessary. Splenectomy may be indicated if there is an associated chronic haemolytic anaemia. A full diet should be given. Institute one of the drug treatments mentioned above. Choose sodium stibogluconate if available. Record the size of the spleen and liver and the leucocyte count during treatment.

Prevention of kala-azar. Full treatment of all cases.

Elimination of dogs if they are known to be a reservoir of infection. Sandflies should be kept down by the use of dicophane (DDT).

Oriental Sores. Cutaneous Leishmaniasis. The infection is universal among natives of endemic areas and in such kala azar is rarely encountered. Oriental sore is commonest on the exposed skin and it first appears as a papule then a macule which ulcerates and spreads leaving on healing a thin scar and an immune individual.

Local treatment. Carbon dioxide snow is useful for small lesions applied for thirty seconds every ten days. Emetine 20 minims of 2 per cent. solution or berberine sulphate 3 ml. of 1 per cent. solution or mepacrine 5 ml. of 10 per cent. solution may be infiltrated round the margin of the sore. Deep scarring may result from x ray treatment and excision or application of caustic gives equally good results. Penicillin is valuable in the presence of gross secondary infection.

General treatment. As for kala azar but the trivalent antimony compound stibophen (Fovadin, Bayer) gives best

results. The initial dose is 1 ml gradually increasing to 3 ml by twice weekly intramuscular injections over eight weeks.

In view of the fact that the sores show a natural tendency toward healing treatment should be cautious. Systemic treatment is as a rule necessary only in extensive and progressive cases especially with facial lesions for which local therapy cannot be given.

Frambesia levis

This is a form of primitive syphilis caused by *Treponema pertenue* which is common in indigenous tropical communities and conveyed by non venereal contact. The integuments are affected but not the viscera or central nervous system. *Treponemata* can be obtained from scrapings of the primary and secondary lesions and the Wassermann and Kahn tests become positive. The disease yields readily to organic arsenicals but not to mercury. Yaws is compatible with good health, mechanical deformity may result from such lesions as synovitis of the knee or mouth stricture.

Treatment. Antibiotics. *T. pertenue* is sensitive to these agents. Two injections with seven days interval of procaine benzylpenicillin in oil with 2 per cent aluminium monostearate is effective (1 200 000 units for adults and 600 000 units for children). The tetracyclines in dosage of 2 G daily for five days may be given in cases where oral treatment is desired.

Arsenic. Neosalvarsamine intravenously was formerly used (0.6-0.9 G). Intramuscular sulpharsphenamine is preferable for children (and 1 ten years 0.3 G and under three years 0.1 G). In early cases a single dose may cure and granulomata usually disappear within ten days. Two or three doses at weekly intervals may be required for tertiary cases and in chronic cases with gross destructive lesions weekly injections should be continued for three months.

Bismuth. The usual preparation is sodium potassium bismuth tartrate which contains 60 per cent of metallic bismuth. It is given intramuscularly in doses of 0.15-0.3 G at weekly intervals and may be combined with arsenicals. Bismuth salicylate can be used also. Stomatitis is a troublesome side-effect.

Management of a case of yaws. 1 Leg ulcers should be cleaned and dressed daily and the limb put at rest

2. For crab yaws the feet should be soaked in a warm sodium carbonate solution. The hyperkeratotic skin is peeled off exposing the papillomata. These are brushed with copper sulphate or perchloride of mercury (1 : 1000). 2 per cent tartar emetic ointment may be used.

3 Commence treatment with penicillin arsenic bismuth or a combination of these. Penicillin alone is simpler and more efficient for mass therapy.

4 Follow the response by repeated Wassermann tests. When the reaction becomes negative repeat once monthly for three months then three monthly for one year. If still positive after six months or relapse occurs the treatment course should be repeated.

5 Treat any concurrent infection particularly malaria or ankylostomiasis.

Relapsing Fever

An insect borne disease due to infection with a spirochaete. The two main types are louse borne relapsing fever due to *Treponema recurrentis* and tick borne relapsing fever due to *T. duttoni*.

Treatment. Tetracyclines, chloramphenicol, penicillin, arsenic and gold have all been used.

The antibiotics particularly the tetracyclines and chloramphenicol are the most effective remedies but are safer if administered during an apyrexial interval. They should be given orally 1.2 G on the first day and then 1 G daily for three to four days. This dose usually prevents relapses. At the onset of a bout of fever neosarsphenamine is very effective. This drug is given intravenously in dosage of 0.01 G per kg body weight. Gold (Solganal, Schering) has been tried in combination with arsenic especially in the tick borne fever which may be resistant to arsenic alone. Initial dose is 0.01 G intramuscularly and the course should not exceed 1 G.

Rat bite Fever

Rat bite fever may be separated aetiologicaly into two specific diseases the spirillar form caused by *Spirillum*

minus and the streptobacillary form caused by *Streptobacillus moniliformis*. The disease may follow the bite of a rat or of animals which have been worrying them.

Treatment. Both types respond equally well to penicillin streptomycin or one of the tetracyclines. Aqueous procaine penicillin 600 000 units given intramuscularly once daily for seven days is sufficient. As a prophylactic measure all rat bites should be cauterised.

Yellow Fever

A mosquito-borne disease of international importance. Vectors are various species of *Aedes* for urban yellow fever and *Haemagogus capricornis* for jungle yellow fever. The monkey is an important reservoir of infection. The incubation period is four to five days and the official quarantine period six days. Persons showing fever on the sixth day are isolated. In endemic areas the disease is usually silent, and manifests itself only in new arrivals who are not immune.

The virus of yellow fever is present in the blood during the first three days of illness and can be cultivated in chick embryo media. A panotropic strain 17 D is used for preparation of vaccine. Being live it loses potency rapidly and distribution is difficult. On injection the virus circulates in the blood but causes no ill-effects and it cannot be transmitted by mosquitoes. It is fully protective from ten days after inoculation up to four years and should be given at least 111 days before arrival in a yellow fever area.

The onset of yellow fever is sudden with rigor, intense headache, rising temperature and falling pulse rate. Vomiting is a prominent feature. After a remission on the third day fever usually recurs and a critical phase develops, which is characterised by jaundice, black vomit, albuminuria and extreme prostration.

Treatment. There is no specific treatment for this disease. Complete rest in bed is essential and the patient should not be transported long distances. As much fluid as possible should be given. If vomiting occurs 3 per cent glucose intravenously should be used. Anaemia is a serious complication and requires appropriate treatment (p. 194). Immune serum is of no value after the onset of fever.

Control of yellow fever 1 *Local control* When a case of yellow fever occurs in an endemic area or is imported into a country where the vector is present the patient should be isolated in a mosquito-proof building and the disease notified immediately. All living-quarters in the area should be sprayed with 5 per cent pyrethrum and the population inoculated.

2 *National control* Endemic areas must be clearly defined and expert diagnostic service made available.

3 *International control* The International Convention makes provision for preventing transfer of infected persons from one country to another and defines infected countries. It requires effective spraying of ships and aircraft with pyrethrum just after leaving an infected country and just before arrival at destinations. DDT should not be used on account of its delayed lethal action on adult mosquitoes.

Dengue

An acute infectious fever due to a virus transmitted by the mosquito *Aedes*. It occurs in epidemics usually at the beginning of the hot season. Onset is abrupt with high fever, bradycardia, post-orbital headache and pains in the bones. The temperature falls but a second bout of fever is usual.

Treatment is entirely symptomatic. A vaccine has been used for prophylaxis but its value is doubtful. Anti mosquito measures should be taken.

Sandfly fever

A virus disease and the vector is *Phlebotomus*. It resembles dengue and occurs in epidemics. After an incubation period of three to seven days there is sudden pyrexia with headache, conjunctival injection and leucopenia. Treatment is symptomatic and anti sandfly measures should be taken as in kala azar.

Rabies

Once the disease develops clinically there is no known cure. The patient should be kept in a darkened room. At first barbiturates may be used for sedation but morphine may give more relief. Spasms are controlled by chloroform.

anaesthesia or curare tubocurarine chloride should be injected in 15 mg doses.

Prophylaxis When a person has been bitten by a dog, wolf, jackal or bat in a country where rabies exists, the following procedure should be adopted.

1. Immediate cautery of the wound with pure ph. nol. The dog should be secured and a search made for other possible victims, especially young children. The animal must not be destroyed. If it is well at the end of ten days anti-rabic treatment of the victims may cease.

2. If the dog has been destroyed by its owner, remove the brain and despatch it to the laboratory for diagnosis of rabies.

3. Commence anti-rabic inoculations immediately. A great number of anti-rabic vaccines are in use. They consist of a suspension of animal nervous tissue containing the fixed virus of rabies. The virus may be either attenuated or killed. Since the dose of each vaccine varies the instructions accompanying the ampoule should be followed. Immunity lasts only three months. Hyper-immune serum (Lederle) is now available and in severe risk cases should be used with the vaccine. Combined vaccine and immune serum therapy is especially indicated for bites involving the head or neck. It is considered most effective if used within forty-eight hours after the bite. Since it is a horse serum product the usual precautions against serum sensitivity should be followed. Anti-rabic inoculations are painful and indurated areas may form at the injection sites. Neurological complications may occur such as transient paraplegia and cranial nerve paralysis (especially of the facial nerve). Acute polyneuritis has been reported which is more serious. Cortisone has been found to hasten recovery from these complications.

Control Strict quarantine of potentially infective animals on importation to rabies-free areas (6 months). Where the dog is the principal carrier, good results have followed mass inoculation of the canine population with vaccine. In countries where wolves and jackals spread the disease, shooting and trapping are used. Where the vampire bat is the vector, the bat population must be kept down and the cattle vaccinated.

Ankylostomiasis

Hookworm disease is a common cause of debility and anæmia in the tropics and it is due to infection with *Ankylostoma duodenale* or *Necator americanus*. Treatment is similar in both infections but *Necator americanus* is more easily eradicated. The larvæ of other hookworms such as *Ankylostoma braziense* may cause ground itch in man without further development.

The outstanding features of hookworm disease are anæmia and œdema of the face and legs. Mild pyrexia is common and the abdomen is distended. There may be retinal hæmorrhages and melæna.

Treatment. Tetrachlorethylene. The most useful drug for this disease. Adult dose 4 ml. for children 0.2 ml. per year of age. Administered in capsule form on empty stomach followed by a saline purge in 1½ hours. May cause toxic jaundice and is contra-indicated in nephritis and hepatic disease.

Hexylresorcinol. The crystals are administered in freshly prepared capsules of 0.2 G. Adult dose is 5 capsules for a child 4 capsules and for children under six years 2 capsules. No food or alcohol should be taken for four hours after treatment. This drug is free from toxicity but gastro-intestinal irritation sometimes arises. Treatment may have to be repeated.

Management of a case of hookworm disease. 1 The most urgent indication is treatment of the inevitable anæmia and iron should be given. For severe anæmia blood transfusion is indicated.

2 When the general condition permits give antihelminthic treatment.

Filariasis

Filariasis includes the following conditions

1 Infection with *Filaria bancrofti*. Vector various species of anopheline and culicine mosquitoes. 2 Infection with *F. malayi*. Vector the mosquito *Mansonioides*. 3 *F. loa* infection. Vector the fly *Chrysops*. 4 Onchocerciasis due to

Onchocercus volvulus Vector the fly *Simulium damnosum*

5 *Dracunculus medinensis* Vector *Cyclops*

F *bancrofti* and *malayi* infections

The microfilariae gain entrance through the skin at the time of the mosquito bite and they show a characteristic periodicity in the peripheral blood being found only when the patient lies down. The following manifestations may occur: elephantoid fever, abscess formation in regional lymph glands, lymph scrotum, elephantiasis of the legs and scrotum, chyluria and chronic synovitis of large joints.

Treatment *Diethylcarbamazine* (Hetrazan, Lederle). Dosage is 6 mg. per kg. body weight daily for twenty-one days by mouth. Urticaria frequently follows.

Management of a case of filariasis. 1 *Early cases not showing elephantiasis.* The patient should be removed from the endemic area to prevent reinfection. Elephantoid fever calls for cold sponging and calamine lotion should be applied to the inflamed lymphatics. Abscesses must be drained and for lymph scrotum or funiculitis a supporting bandage is required. If secondary skin infection appears, sulphonamides or penicillin should be used. A course of diethylcarbamazine is instituted.

2 *Elephantiasis.* Due in part to lymphatic obstruction but secondary infection and allergy are believed to have some influence. Surgery is indicated in advanced cases. Large scrota should be removed preserving the genitalia. Large masses of elephantoid tissue are best excised.

Loiasis. Clinical manifestation is the Calabar swelling and the adult worm may migrate to the eye. For sub-conjunctival worms cocaine and adrenaline should be instilled, the worm immediately transfixed with forceps, and a silk suture tied underneath. The conjunctiva is then snipped with scissors, the worm removed and the conjunctiva sutured. If the worm eludes capture it can be made to reappear by sponging the eyelids with warm water.

Diethylcarbamazine is the most specific treatment. To avoid dangerous allergic reactions, begin with 100 mg. and increase by this amount daily, give 400 mg. on fourth to tenth days.

Onchocerciasis

Common in West Africa but occurs in South America

Onchocercus volvulus has been called the blinding worm as it is an important cause of iridocyclitis. The adult worms live in nodules on the body surface and the microfilariae have an affinity for the eye.

Treatment All nodules must be removed under local anaesthesia in order to prevent eye involvement. The best drug is suramin intravenously in five to ten weekly doses of 0.5 G. It is particularly effective in ocular cases. Diethyl carbamazine may also be used but is less effective.

Dracontiasis

The guinea worm is acquired by ingestion of *Cyclops* (a small water insect) infected with the embryo of the worm. The male adult worm is rarely seen but the female is of great length and inhabits the subcutaneous tissues. Penetration of the skin usually occurs on the leg which is frequently in contact with water. A supply of embryos can be obtained by allowing cold water to trickle over the point of exit of the uterus of the worm.

Treatment There is no satisfactory chemotherapy. The worm should be removed without sepsis. The patient is put to bed to prevent swelling and accidental injury to the worm which will result in infection. As soon as the worm protrudes tie a silk ligature round it and fasten to a small stick one turn of the stick daily will extract it. The time occupied is about two months. Sulphonamides or penicillin should be used if sepsis supervenes and incision may be necessary.

The worm may be removed surgically by making a series of incisions across it pulling out loops with a hook and cutting them off.

Prevention of infection Drinking pure water or boiling doubtful supplies.

Schistosomiasis

Three schistosome flukes cause disease in man

1 *Schistosoma haematobium* Originally an African parasite it has spread to Palestine, Crete and Portugal.

Hæmaturia aggravated by exercise may occur. Complications cystitis calculi hydronephrosis fistula stricture penile elephantiasis salpingitis and vesical carcinoma. Other manifestations are bilharzial pneumonia dysentery (due to colonic involvement) and severe anaemia.

2 *Schistosoma mansoni* Found in Africa and N. and S. America. Interlobular pipe stem cirrhosis of the liver causes ascites. An acute dysenteric syndrome and polyposis are common. Splenomegaly is marked. Profound anaemia complicates African infections.

3 *Schistosoma japonicum* Occurs in China, Japan and the Philippines. Causes severe cercarial dermatitis, dysentery, cirrhosis of the liver and splenomegaly.

Treatment 1 *Tartar emetic sodium antimonyl tartrate*. A specific cure. Used as a freshly prepared 2 per cent solution intravenously by slow injection. Commence with 30 mg. and increase by this amount on alternate days until 150 mg. is reached. A course consists of 2 G. Toxic symptoms especially coughing and vomiting are common. The other drugs unfortunately are less effective.

2 *Lithium antimony thiomalate* (Anthiomaline M & B). Used as a 6 per cent solution intravenously or intramuscularly. Commence with 0.5 ml. and increase on alternate days until 2.5 ml. is reached. The total required for cure is about 50 ml.

3 *Subophen* (Fouadin). This trivalent antimony compound is used in 7 per cent solution intramuscularly. The initial dose is 0.5 ml. which should be increased on alternate days to a maximum of 5 ml. A course consists of 50 ml.

4 *Emetine*. Useful in antimony resistant cases. Commence with gr. 4 intramuscularly and follow with gr. 1 weekly for fifteen to twenty doses.

Management of a case of schistosomiasis. 1 Institute specific therapy preferably with tartar emetic. Emetine may be better in *Schist. japonicum* infections. Antimony should be used with extreme caution in cases showing liver cirrhosis, pulmonary involvement or cerebral manifestations. Emetine is safe in such circumstances.

2 Symptomatic treatment paracetamol abdomen iron

Criteria of cure Intestinal amebiasis is essentially chronic and negative stool reports are untrustworthy. After treatment six consecutive stools are examined for cysts and repeated at three monthly intervals for a year. Salines should be given to ensure liquid stools which must be examined while fresh.

Management of a case of amebiasis. Confine the patient to bed for the first fortnight of treatment. If severe give fluid diet. Treat bacillary dysentery if present. Give a standard course of drug treatment. During convalescence increase the diet but avoid roughage. Perforation of the bowel requires surgical intervention.

Amebic hepatitis. Chloroquine has proved superior to emetine. The dose is 15 G base six hourly for four days then twice daily for eight days tailing off with one dose daily for nine days. An antibiotic should be given concurrently. A course of E 1 or Diodoquin should follow to rid the bowel of residual infection. If fever and leucocytosis persist in spite of this treatment abscess formation is likely and aspiration or open operation indicated.

Bacillary Dysentery

Bacillary dysentery is an epidemic disease and its incidence is directly related to the fly season. Complications are rare but in chronic and relapsing cases there is a tendency to the development of sprue. Shiga infections are usually severe whereas cases due to the Sonne group are mild. Flexner infections tend to be intermediate in severity.

Treatment Sulphonamides. The little absorbed sulphonamides are eminently successful in bacillary dysentery and have ousted earlier methods of treatment. The adult dose of succinylsulphathiazole is 10-15 G in five divided doses daily for three days followed by one third to one half dosage for three to five days. Phthalylsulphathiazole is used in dosage of 3-4 G daily for three days followed by half-dosage for a further three days. Small doses of an absorbable sulphonamide e.g. sulphadiazine should be given as well.

The *tetracyclines* sterilise the stools in a few days and are especially useful for children. These should be continued until the temperature is normal for two days. The total daily

dose of oxytetracycline for a child is 20 mg per lb body weight given in divided doses six hourly

Management of a case of bacillary dysentery 1 Absolute rest in bed Dispatch a specimen of stool or rectal swab for bacteriological diagnosis

2 Liberal fluids as in typhoid fever in severe cases intravenous fluids may be necessary Return to solid food must be gradual

3 Commence antibiotic treatment immediately

4 Symptomatic treatment Gripping abdominal pain is best relieved by the application of warmth to the abdomen

For chronic cases preliminary sigmoidoscopy and bacteriological examination should be done as many are amebic

Balantidial Dysentery

A rare disease caused by infection with *Balantidium coli* Pigs are a reservoir of infection and swine herds provide most of the cases

Clinically it produces a chronic intractable dysentery

Stovarsol 1 g daily by mouth for ten days is effective

The tetracyclines (0.5 G every six hours for 10 days) are probably better

Cholera

An acute infection characterised by severe diarrhoea and vomiting associated with collapse water and salt depletion leading to uraemia Clinically the disease is divided into three stages (1) rice-water stool evacuation (2) collapse with cyanosis and dehydration (3) reaction marked by fever and re-establishment of urinary secretion.

Treatment is essentially a matter of maintaining the fluid and electrolyte balance There is no specific treatment Sulphonamides are of doubtful value

Management of a case of cholera. A record of temperature pulse rate blood pressure and blood specific gravity should be kept

First stage 1 Ensure complete rest and maintain warmth by hot water bottles or electric cradles.

Give as much fluid as possible by mouth.

Second stage 1 Give hypertonic saline intravenously (2 N sodium chloride) The infusion should be done slowly and

stopped temporarily if headache occurs. The amount required varies with the blood specific gravity but it should be continued until normal (1058) is reached when isotonic saline may be substituted.

2. If urinary suppression occurs the treatment outlined for this complication should be adopted (p. 194).

Third stage 1. If the skin temperature exceeds 103.5 F cold sponging is indicated.

2. Intravenous drip (glucose saline) may be continued or salines given by the rectal route.

3. If the blood pressure remains below 100 mm Hg / noradrenaline should be added to the transfusion fluid (p. 34).

Return to normal diet must be cautious and protein limited until renal function is regained. Bed rest is maintained for two weeks after symptoms have disappeared owing to the danger of sudden collapse.

Control of cholera 1. Protection of food and water from contamination. A chlorinated water supply is safe provided it contains free chlorine. Wells should be treated with bleach powder.

2. Rigorous isolation of patients and disinfection of dejecta with 5 per cent cresol. Feeding utensils should be boiled and soiled clothing etc. soaked in 2 per cent cresol.

3. Cholera inoculation should be given to everyone in the area or entering it. Initial dose of vaccine (freshly prepared) is 0.5 ml (4 000 million) followed in ten days by 1 ml subcutaneously. The resultant immunity lasts about six months and is by no means absolute.

Leprosy

This disease is now confined almost entirely to tropical climates although small foci remain in Europe e.g. Norway. It may be acquired in many ways—by skin contagion or by infection of the nasal mucosa. Flies may disseminate infection. Infectivity is not high.

Nodular leprosy commonly affects the face. The nodules ulcerate and discharge infectious material. Nerve leprosy is characterised by areas of anaesthesia and skin lesions due to

lepromatous involvement of nerve trunks. The ulnar nerve is usually thickened. Diagnosis is made by examination of nodular discharge, skin sections or nasal smears. The Wassermann reaction may be positive.

Treatment. *Dapsone* (DDS). The standard therapeutic agent which has replaced its disubstituted derivatives such as solapson, whose action depends on the DDS they form in the body. It is rapidly absorbed and slowly excreted. The dosage schedule is 100 mg. twice weekly orally during the first month, 100 mg. three times weekly during the second month and 100 mg. four times weekly during the third month. Reduce the dosage if reaction or anemia occurs, but continue for at least two years. ACTH or cortisone is useful in treating severe lepra reactions. Hydrocortisone eye drops (1 per cent) are of value in the treatment of acute leprous ocular reactions.

Thiosemicarbazone and *streptomycin* are used to supplement DDS or replace it for a time. The adult dose of TB1 is 100 mg. daily for six days during the first week, and 200 mg. daily for six days each following week, allowing an interval of fifteen days each month. It is effective in healing chronic skin lesions. *Streptomycin* suppresses ocular inflammation.

Chaulmoogra. The oil may be given by mouth in doses of 15 minims, gradually increased to 1 drachm. This drug is now seldom used since better results are obtainable with modern chemotherapeutic agents.

Plague

Plague is primarily an enzootic disease of rats and is transmitted by the rat flea *Xenopsylla cheopis*. The human flea *Pulex irritans* can maintain infection from man to man. Bubonic plague manifests itself by sudden high fever, vomiting and mental confusion, and the condition may resemble typhus. The spleen is enlarged and a bubo occurs. If suppuration supervenes, healing of the bubo will be delayed for about one month. The onset of pneumonic plague is also abrupt, with fever, cough, dyspnea and cyanosis. The mortality is high. Diagnosis is confirmed by isolation of *Pasteurella pestis* from blood, buboes or sputum.

Treatment *Sulphonamides* Sulphadiazine is the most effective preparation 4 G should be given at the outset and may be divided between the intravenous and oral routes. Thereafter 0.3 G is given four hourly until the temperature becomes normal. At least four pints of fluid should be taken daily during this course. In fulminating septicæmic cases the initial intravenous dose of sulphadiazine should be 0.1 G per kg. body weight repeated in six hours. Glucose saline by intravenous drip is also useful.

Streptomycin Intramuscular injection of 0.5 G six hourly until the temperature settles thereafter twice daily for five days. Chloramphenicol or the tetracyclines may be used in combination with streptomycin.

Anti plague serum Should be used in the early stage in dosage of 30-40 ml into vein or muscle. Results are variable.

Management of a case of plague 1 Isolate the patient and disinfect his clothing by steam or 10 per cent DDT powder.

2 Nurse in a well ventilated room or ward. An opertient is useful at the outset. For delirium cold sponging is soothing but morphine should be given if necessary.

3 Commence sulphadiazine streptomycin therapy. Serum may be given also.

4 Apply ice bags to the bubo. glycerin and belladonna helps to relieve pain. Suppuration is met by incision.

Control of plague 1 Strict isolation of cases in plague hospitals. Nurse pneumonics in a separate ward. Attendants should wear vermin proof garments and the staff and all contacts should be vaccinated.

2 During an epidemic it may be necessary to evacuate an area after disinfestation of the population. Ten per cent mixture of DDT in talc is used for flea control.

3 Movements of individuals out of an infected area should be limited and subject to production of a valid vaccination certificate and to dusting with DDT. Merchandise particularly cotton and rags must be disinfected before despatch from the area.

4 Rat control. Rats can be destroyed by traps or poison.

Brucellosis

An infection characterised by numerous pyrexial relapses with headache joint pains and leucopenia Drenching sweats occur with each deservescence and the spleen may be palpable In children it may take the form of an obstinate and featureless pyrexia Three organisms cause this disease (1) *Brucella abortus* which naturally infects cattle and is found in cows milk (2) *Brucella melitensis* which is transmitted by goats milk (3) *Brucella suis* which is transmitted to man by handling infected pork Infection can occur through the skin and farmers veterinarians and abattoir workers experience a high incidence

Treatment The tetracyclines are sometimes effective in dosage of 2 G daily for twenty-one days The addition of intramuscular streptomycin 1 G daily for the first two weeks may increase the cure rate After cessation of treatment relapses are frequent in which case the treatment course should be repeated Gost reports excellent results from novobiocin (Cathomycin Merck Sharp & Dohme) 0.25 G orally four hourly until the day after deservescence and then six hourly to a total of 18 G

The Typhus Fevers

The following varieties are recognised 1 Classical typhus due to *Rickettsia prowazekii* and transmitted by the louse *Pediculus humanus* The patient's serum agglutinates the OK 19 strain of Proteus 2 Murine typhus (Brill's disease) transmitted by the rat flea it is essentially endemic 3 Tick typhus of which there are many types such as rocky mountain spotted fever caused by *Rickettsia rickettsii* and transmitted by the tick *Dermacentor andersoni* and *fièvre boutonneuse* transmitted by the dog tick *Rhipicephalus sanguineus* 4 Mite-borne typhus (scrub typhus) due to *Rickettsia orientalis* and transmitted by mite larvae

Classical Typhus. World wide distribution and epidemics are common in conditions of war and famine Infection is acquired by contamination of louse bites or scratches by faeces or body juices of infected louse The onset is sudden with rigors, headache vomiting and fever The rash appears

on the fourth or fifth day delirium tremors and deafness are common

Treatment Chloramphenicol is specific Give an initial oral dose of 3 G then 0.25 G at three hourly intervals The tetracyclines have also given good results Dosage 2 G orally followed by 0.5 G six hourly

Control of classical typhus. Two vaccines are available (a) Cox's (killed *R. prowazekii*) 1 ml weekly for three doses Reduces the severity of the disease (b) Blane's (live vaccine prepared from dried flea faeces) dose = 1 ml May cause mild murine typhus in some cases During epidemic prevalence vaccination should be general It is specially important for personnel of isolation hospitals They should be provided with vermin proof clothing and be dusted with DDT weekly

Sprue

Sprue affects white residents in tropical countries but is rare among indigenous populations It may not arise until after many years tropical residence and may be silent until the individual has returned to a temperate climate Chronic dysentery is an important predisposing factor and there is a background of vitamin B lack Prominent features are macrocytic anaemia steatorrhoea with excess of split fats loss of weight and sore tongue Remissions are characteristic and tetany may occur in severe cases

Management of a case of sprue 1 Keep the patient in bed and continue with his usual diet until the diagnosis has been confirmed A fractional test meal full blood count and faecal fat analysis should be done

2 Prescribe a diet rich in protein and vitamins but poor in fat Milk = well tolerated and lean meat chicken and eggs are acceptable Fruits may be given freely Carbohydrate is added later Gluten free bread should be used if available

3 Injections of = crude liver extract (Plexan Glaxo Campolon Bayer) 2 ml daily intramuscularly for two weeks and then 2 ml weekly until the erythrocyte count reaches normal This need not be continued indefinitely as in pernicious anaemia but relapse must be met by further injections Vitamin B₁₂ may be effective

4 Folic acid given in dosage of 15-30 mg daily causes considerable symptomatic improvement but may not correct the anemia

5 Nicotinic acid amide 100 mg and riboflavin 5 mg. daily are useful for sprue mouth and tongue

6 Antibiotics or adrenal corticosteroids may be temporarily helpful in some cases but their prolonged use is probably harmful

7 If tetany occurs give 10 ml of 10 per cent calcium gluconate slowly intravenously Bleeding due to hypoprothrombinemia is corrected by vitamin K or its analogue menaphthone 20 mg intramuscularly

Sprue sufferers should leave the tropics permanently

Snake Bites

Snake bite is a common occurrence in tropical practice and remedies should be readily available as the outcome depends on early treatment When examining the wound look for two fang punctures which indicate the bite of a poisonous snake Bites from colubrine snakes (cobras and kraits) cause death by paralysis and asphyxia Cobra venom is also hemolytic, and hemoglobinuria may occur Bites by viperine snakes (Russell's viper and rattlesnake) cause swelling and petechial mottling of the limb also nausea vomiting and syncope

Treatment of snake bite 1 If the snake has been killed secure it for identification

2 Apply a tourniquet at the top of the affected limb and this may be kept in position for twenty to thirty minutes

3 Inject antivenom at a distance from the wound Antivenoms are available against viperine and colubrine bites, also polyvalent preparations They may be used intravenously or intramuscularly The required dose is in inverse proportion to body weight and the dose for a child is several times that required for an adult The usual adult dose is 100-300 ml

4 Suck as much venom as possible out of the wound and incision may be a desirable preliminary Permanganate application is of little value and cauterization is contra indicated

5 Keep the patient quiet in bed Black coffee or caffeine may be given but morphine is harmful

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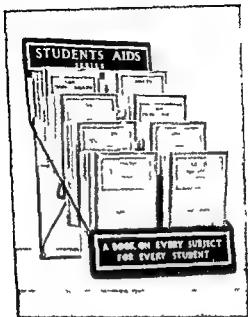
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